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WHO CHRONICLE

VOL. 15, No. 1 - JANUARY 1961

International work in cholera
Malaria eradication in Africa
Antimicrobial therapy of tuberculosis
Laboratory research on the poliomyelitis virus
Simian malaria
Executive Board: twenty-sixth session

WORLD HEALTH ORGANIZATION
PALAIS DES NATIONS
GENEVA

The World Health Organization (WHO) is one of the specia ized agencies of the United Nations. Through this organization, which came into being in 1948, the public health and medical professions of more than 100 countries exchange their knowledge and experience, and collaborate in an effort to achieve the highest possible level of health throughout the world. WHO is not concerned with problems which individual countries or territories can solve with their own resources. It deals, rather, with problems which can only be satisfactorily solved through the co-operation of all, or certain groups of, countries—the eradication of diseases such as malaria, the control of cholera, plague, yellow fever, smallpox and rickettsiosis. Progress towards better health throughout the world also demands international co-operation in many other activities : for example, setting up standards for biological substances, for insecticides and insecticide spraying equipment ; compiling an international pharmacopoeia ; drawing up international sanitary regulations ; revising the international lists of diseases and causes of death ; assembling and disseminating epidemiological information ; recommending non-proprietary names for drugs ; and promoting the exchange of scientific knowledge. In many parts of the world, there is need for improvement in maternal and child health, nutrition, nursing, mental health, environmental sanitation, public health administration, professional education and training, and health education of the public. Thus a very large share of the Organization's resources is devoted to giving assistance and advice in these fields to countries and territories whose health services are in an early state of development and which are therefore weak points in the common front against disease.

- ***WHO Chronicle***

  published by WHO for the medical and public health professions, provides a monthly record of the principal health activities undertaken in various countries with WHO assistance. It also contains summaries and detailed accounts of the other publications issued by the Organization.
  The Chronicle is published in English, French, Spanish, Russian and Chinese.

- ***Bulletin of the World Health Organization***

  contains technical articles, in English or French, contributed by physicians and scientists engaged in public health work. It appears monthly and each issue runs to about 120 pages.

- ***World Health***

  an illustrated magazine for the general public, aims at giving an idea of WHO activities throughout the world and at showing some of the more striking aspects of public health work.
  This publication appears every two months in English, French, Spanish and Portuguese.

Other WHO publications: the *Technical Report Series*, the *Monograph Series*, the *Epidemiological and Vital Statistics Report*, the *International Digest of Health Legislation*, etc., are described in a catalogue which can be supplied free of charge on request.

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3 *International work in cholera—1*

11 *Malaria eradication in Africa*

17 *Antimicrobial therapy of tuberculosis*

21 *Laboratory research on the poliomyelitis virus*

23 *Simian malaria*

26 *Executive Board: twenty-sixth session*

29 *Notes and news*

35 *Review of WHO publications*

WORLD HEALTH ORGANIZATION

In this issue

- *Although there was nobody from whom they could have contracted it, two staff members of the US National Institutes of Health, suddenly went down with malaria in May 1960, while rhesus monkeys were being inoculated with* P. cynomolgi bastianelli *sporozoites. These were the first proven cases of transmission of simian malaria to man, and further experiments on human volunteers confirmed the transmissibility. Monkeys are widespread in many parts of the world, and this discovery raises the possibility—hitherto discounted—that animal reservoirs play a part in the transmission of malaria. A WHO Advisory Committee on Medical Research that met in June 1960 felt that the discovery was unlikely to affect malaria eradication campaigns, but that it deserved further study. It also opens up new possibilities in chemotherapeutic research (see page 23).*

- *Only five years ago the prospects of eradicating malaria in Africa appeared to WHO experts " not quite so promising ". A survey in 1959 found the prospects more encouraging, but many difficult technical, economic and administrative obstacles have still to be overcome (see page 11).*

- *The treatment of tuberculosis with streptomycin and PAS as evolved 15 years ago has revolutionized the management of this disease. A look at experience with these and newer antituberculosis agents, such as isoniazid, suggests that there may come a time when most tuberculous patients will be treated at home (see page 17).*

- *One of the great unknowns of oral poliomyelitis vaccination is the fate of the viruses, attenuated when they are administered but then released into the community and thereafter free from all control. Various methods have been worked out to distinguish the pathogenic virus from the vaccine virus. A study of these methods shows the intricacy of the problems that must be solved to ensure that polyomyelitis virus vaccine is harmless (see page 21).*

- *The dread of cholera contributed more than any other single factor to bringing governments together in a common effort to conquer disease. Although cholera occurs today only in limited endemic areas, mostly in India, public health workers must be prepared to meet emergencies and deal with sporadic outbreaks. This issue contains the first of several articles that together will outline in compact form the latest knowledge about the disease and the main lines of international work since 1948 (see page 3).*

INTERNATIONAL WORK IN CHOLERA

1. Past and present distribution of cholera *

The term "huo luan", the present name for cholera, is found in the Nei Ching and other old chronicles, but it appears that it does not refer to the disease we now recognize as cholera. There is little doubt that in the past this term has been used to cover a group of affections . . . and cholera might have been mixed up with them. A significant point, however, is that no one, until a late period, alludes to the epidemic character of the disease.

WONG & WU LIEN-TEH [1]

The vast pandemics of cholera that swept across Asia, Europe and the Americas during the nineteenth century marked a sudden transformation in the character of a disease that appears to have been endemic in parts of Asia for centuries. Indeed, it is probable that cholera has been present in India, in the region of the Ganges delta, since time immemorial. The clinical manifestations of the disease may be closely imitated, however, by other gastro-intestinal infections, and it is therefore difficult to identify it with certainty from early descriptions of diarrhoeic diseases.

An epidemic among the Athenians, described by Thucydides in the fifth century B.C., may have been true cholera, since it is stated that the contents of the bowels ran out "like pure water", but in general the early Greek writers mention bilious discharges, and the word χολέρα found in Hippocratic writings is thought to refer to a disease different from that now recognized as cholera. Similarly, much uncertainty exists regarding the interpretation to be placed on descriptions of cholera-like diseases to be found in ancient Indian medical literature. There is evidence that in Lower Bengal the people have long worshipped a goddess of cholera, coming from all parts of the country to Calcutta to pray at her shrine. This suggests that the disease must have raged at times with considerable violence. Suśruta, an Indian physician of the seventh century A.D., has described a disease characterized by diarrhoea and vomiting, stabbing pains, cyanosed lips and nails, sunken eyes, and a weak voice. Although this closely fits the clinical picture of cholera, there is nothing to indicate that it refers to the epidemic form of the disease, commonly known today as Asiatic cholera.

On the other hand, from the sixteenth century onwards, detailed descriptions of cholera in India were given by European observers, the earliest referring to the province of Goa, on the west coast of India, where the first Portuguese landings were made. During the seventeenth century, Dutch, French and British observers reported epidemics from other areas of the west coast, and by the last quarter of the eighteenth century the disease had been encountered on the east coast as well, and even beyond the confines of the sub-continent.

It seems likely that early importations of cholera took place from India into neighbouring countries, particularly into Burma, and it is claimed that in 1669 it was carried into China. The first reliable reports of cholera outside India relate to an epidemic in Ceylon in 1782, severely affecting the British fleet anchored at Trincomalee, and to an outbreak in Burma in 1783. At the same time an

* This is the first of a series of articles intended to give a concise account of the public health aspects of cholera, and to outline present trends in its control. Those wishing to go more deeply into the subject are referred to a comprehensive monograph recently published by WHO: *Cholera*, by R. Pollitzer (with two chapters written in collaboration with W. Burrows and S. Swaroop), Geneva, 1959 (*World Health Organization: Monograph Series*, No. 43), 1019 pages.

[1] Wong, K. C. & Wu Lien-teh (1936) *History of Chinese medicine . . .*, Shanghai

epidemic was raging on the right bank of the Ganges in north-west India, killing 20 000 pilgrims in less than eight days at the holy town of Hardwar. During the remainder of the eighteenth century, there were frequent reports of epidemics in various parts of India, often involving European troops, and there was a violent outbreak in Bengal in 1814. Ceylon was again affected in 1804.

Cholera becomes pandemic

In 1817, cholera suddenly flared up with hitherto unprecedented virulence and began to spread to parts of Asia that had previously been free from the disease. This violent eruption is believed to have had some connexion with the unusually heavy rainfalls and disastrous floods of 1815 and 1817, and the fact that the intervening year, 1816, was excessively hot and dry. Probably originating in the hinterland of Bengal between the Ganges and Brahmaputra, the epidemic had reached Calcutta in early August, and a month later the magistrate of the city reported that it had been "far more fatal than at any former period within the recollection of the oldest inhabitants". Within three months the whole of the province of Bengal—nearly 200 000 square miles in area—had been affected, scarcely a single town or village escaping the ravages of the disease. The infection also overran the Bundelkhand, to the south of the former United Provinces, causing great havoc among troops stationed in the area.

In 1818, the disease extended north-eastwards into Nepal, westwards into Bombay, and south into Hyderabad, Mysore and Madras. Towards the end of the year, it reached Trincomalee in Ceylon, spreading over practically the whole island during the following year. Burma also appears to have been invaded by the land route in 1819, and epidemics of sea-borne cholera broke out in 1820 in various parts of the Malay peninsula as well as in Java, Borneo and other islands of the Indonesian archipelago. At the same time, the disease reached several ports in China, spread along the Yangtze valley, and invaded the north of the country the following year. Further outbreaks occurred in northern and central China in the period 1822-24. The disease first appeared in Japan in 1822, exacting a terrible toll of lives in Osaka and some other cities.

A British expeditionary force sent from India to Oman in 1821 carried the infection to Arabia. From Oman, cholera spread up the Persian Gulf into what is now Iran and across to the southern shore of the Caspian Sea. At Basra, in present-day Iraq, it killed more than 15 000 people in less than three weeks. Carried up the Tigris by boat and caravan, the disease caused terrible havoc among the Persian army attacking the city of Baghdad. The following spring, cholera broke out along the Euphrates as well as the Tigris and eventually reached Tiflis and Astrakan on the Caspian Sea. There the pandemic came to a halt, as a result, it is believed, of the severe winter of 1823-24.

Cholera crosses the Atlantic

In the meantime, the original epidemic in India had also subsided. The respite was short-lived, however, and by 1826 cholera was again showing signs of increased violence and activity in Bengal. By 1829, it was rampant in Afghanistan, penetrated again into Persia, and was also present around Bukhara and Khiva. From there, it seems to have been carried by caravans to Orenburg in the south-east corner of European Russia and soon started to spread north-eastwards. The second great pandemic was under way. In the spring of 1830, cholera began to advance on a wide front, ultimately invading not only most parts of Europe but also large parts of the Americas, as well as Arabia and East and North Africa. In spite of rigid quarantine measures, by 1831 the disease had progressed as far north as Archangel in Russia and entered Finland. Poland, Austria and parts of Germany were affected in the same year, and ships carried the infection from the Baltic ports to England, where a number of outbreaks occurred in late 1831 and 1832. In the latter year, cholera not only broke out in Ireland, France, Belgium and the Netherlands, but also crossed the Atlantic and appeared in Canada and the USA. Subse-

quently, it spread into Mexico and other countries of Central and South America. In Europe, recrudescences of the disease continued every year until 1837. Spain was affected in 1833, in spite of exceptionally severe quarantine measures, and from there cholera spread along the southern shores of France and into Italy and Switzerland. In 1834 and 1835, French troops carried the disease into Algeria. Outbreaks had already occurred in Egypt, as well as in Syria and Palestine, in 1831. These are believed to have been started by pilgrims returning from Mecca, where cholera had taken a heavy toll of life earlier that year.

In India, fresh outbursts of cholera occurred in Lower Bengal in 1827 and again in 1840. Troops that had been assembled in Calcutta and Madras carried the disease in 1840 to the Straits Settlements and China, where the pandemic raged with great ferocity during the next two years. A further serious recrudescence of cholera in Lower Bengal in 1845 was followed by the invasion of Madras and Ceylon on the one hand, and of the Bombay area on the other. From there the disease spread westwards and in 1846 invaded almost the whole of the Arabian peninsula. The following spring, cholera again appeared along the shores of the Caspian and the Black Sea and advanced rapidly across Russia. After a lull during the winter, it resumed its march early in 1848, reaching Norway in the north, the Balkan countries in the south, the British Isles in the north-west and Spain in the south-west. Pilgrims returning from Mecca once more imported the disease into Egypt, and it also reappeared in the USA. During 1849, it overran practically the whole of the States lying east of the Rocky Mountains, made inroads into Canada and was carried into Mexico and Panama. In 1850 and again in 1851, cholera raged with great violence in Cuba and Jamaica.

The second pandemic had barely subsided when a fresh pandemic broke out in 1852, attributed by some to the persistence of a focus of infection in Poland, but undoubtedly reinforced by fresh waves of infection from India. This pandemic lasted until the end of 1859, affecting at first mainly Europe and North America. In 1855, the infection spread from Arabia into Syria and Asia Minor and also appeared in Egypt and other parts of North Africa. Furthermore, while North America now remained apparently free, cholera broke out in Venezuela and Brazil. China and Japan suffered severely during the period 1857-59, and in the latter year a serious recrudescence of the infection in Bengal was followed by a fresh wave of infection in Russia and various parts of Europe.

New traffic routes spread cholera

The fourth pandemic, which began in 1863, differed from the first three in that the disease penetrated into Europe by new traffic routes, via Arabia into Egypt, Constantinople, southern France and Italy. In May 1865, cholera broke out with extreme violence at Mecca, where some 90 000 pilgrims were assembled for the jubilee year. It has been estimated that at least one third of them fell victims to the disease. Returning pilgrims disseminated the disease in various parts of Arabia, Iraq, Syria, Palestine and Egypt. From Alexandria, the infection was carried to Istanbul, Marseilles and other Mediterranean ports. Cholera appeared at widely scattered points in Europe during 1865 and 1866, the most serious ravages being in Russia, Germany, Austria-Hungary, Italy, Belgium and the Netherlands. Between 1866 and 1873, sporadic outbreaks of limited extent were of frequent occurrence throughout Europe, and a number of major epidemics also occurred, particularly in Russia. In the meantime, the disease had been spreading southwards from Abyssinia into Africa. By 1869, it had reached the region of Kilimanjaro, and from there it advanced south-westwards across Lake Tanganyika to the upper reaches of the Congo, and south-eastwards to Zanzibar island, where 70 000 persons succumbed to the disease in 1869. By May 1870, cholera reached the city of Mozambique and was then carried to the Comoro Islands, Madagascar and the Seychelles. Cholera was also rife in the north of Africa, and Morocco had a violent outbreak in 1868. It seems likely that caravans carried it from there to French West Africa,

and thence the infection spread to Gambia and Portuguese Guinea.

Cholera was rampant in New York in 1866 and the newly built railways facilitated its spread to other parts of the USA. Large-scale troop movements also assisted the dissemination of the infection. Nevertheless, the number of deaths was far lower than in earlier pandemics. Canada remained almost free from the infection, but the disease made several appearances in Central and South America from 1866 to 1868. In the USA a serious recrudescence of the disease occurred in the area of New Orleans and the Mississippi basin in 1873.

Cholera raged with particular violence in India in 1875, and other Asian countries also suffered severely during the concluding years of the pandemic. Information is scanty regarding the fate of countries to the east and south-east of India at this time. Cholera is stated to have been widespread in China in 1862, in the Indonesian archipelago in 1863 and 1864, and in China and Japan in 1864-65. Serious outbreaks also occurred in Japan in 1877-79.

The pandemics decline

The fifth cholera pandemic, which lasted from 1881 to 1896, caused much less havoc than its predecessors, although wide areas were affected. It was during this pandemic that an important advance was made in the study of the disease: Koch succeeded in proving that cholera is caused by a specific gastrointestinal infection. As in the case of the previous pandemic, the infection was first disseminated by pilgrims returning from Mecca, where epidemics occurred in 1881 and 1882 following a serious exacerbation of the cholera situation in India. In 1883, cholera broke out in Egypt among visitors to a fair at Damietta and soon spread to other parts of the country. Between 1884 and 1890, a number of epidemics occurred in France, Italy and Spain, but the rest of Europe remained practically free from the disease. The failure of cholera to become entrenched in Great Britain at this time was attributed to adequate preventive measures and the provision of wholesome water supplies.

The spread of cholera to the USA was narrowly averted in 1887 by rapid laboratory diagnosis of the disease among the passengers of a steamer from Marseilles—the first occasion on which use was made of bacteriological methods in combating the scourge. Serious outbreaks took place, however, in Argentina and in Chile between 1886 and 1888.

In 1892, cholera flared up in Afghanistan and Persia and spread rapidly across Russia, claiming some 800 000 victims in 1893-94. At the same time, an explosive outbreak occurred in Germany at Hamburg, owing to the distribution of unfiltered water from the River Elbe. Sporadic cases of cholera also occurred at many other places in Germany as well as in France between 1892 and 1894.

Throughout the pandemic, cholera continued to be prevalent in India, and there were repeated epidemics in the Indonesian archipelago, as well as in China and Japan.

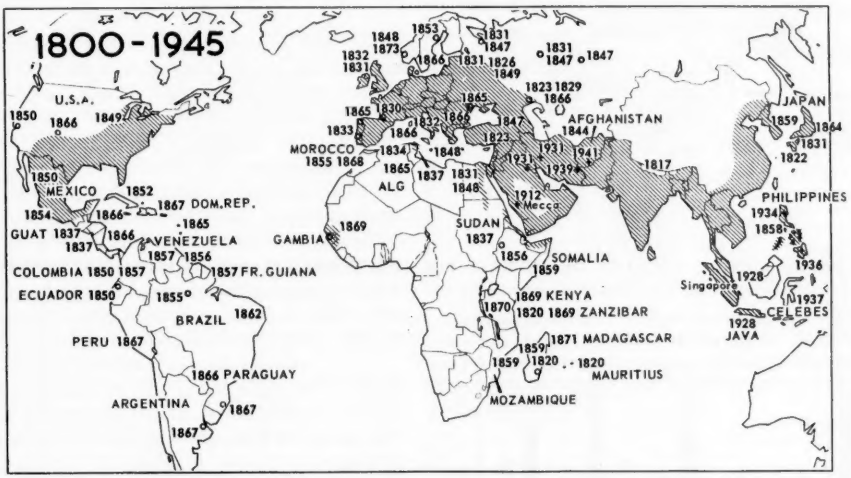
An increase of cholera in India in 1899 ushered in a new pandemic which lasted until 1923. Violent outbreaks occurred in Calcutta and Bombay in 1900, with extensions of the disease westwards into Afghanistan and the Persian Gulf area and eastwards into Burma and Malaya. By 1902, the pandemic had spread to the Philippines, Korea, Manchuria, China and Japan. In the same year, pilgrims assembled at Mecca were once again struck down in large numbers and despite every precaution the disease was carried back into Egypt where it claimed 34 000 victims in three months. In 1904 cholera spread from Baku on the Caspian Sea into Russia and during the next few years gradually extended its hold on the country. In 1910 there were over 230 000 cases with almost 110 000 deaths, but for the next ten years the disease tended to be sporadic, with slight exacerbations in 1915, 1918 and 1920. There was a sudden flare-up in 1921, with more than 200 000 cases, but thereafter the disease declined, and in 1924 and 1925 there were only a few sporadic cases. Since then Europe has remained free from cholera.

This sixth pandemic was much more limited in extent than its predecessors. The Americas escaped entirely and in western Europe only sporadic cases or abortive outbreaks occurred.

On the other hand, the pandemic assumed serious proportions at times in central and south-eastern Europe. Thus, frequent and often serious outbreaks occurred in the Balkan peninsula, where the spread of infection was facilitated in 1912 and 1913 by local wars and later by the First World War.

There are some areas that remained unaffected by any of the six pandemics. These are especially the northernmost and southernmost parts of the globe. Thus, in western Europe, Iceland, the Faeroe, Shetland, and Orkney Islands, the Hebrides, Norway north of Bergen, and Lapland were spared. So also were northern Siberia and Kamchatka, Greenland, and the regions of North America beyond the 50th parallel. Similarly, the southernmost parts of Chile and Argentina remained free from the disease, as did the southern parts of Africa. It does not appear that any of the pandemics ever reached Australia and there is no reliable evidence that the islands of the Pacific were affected, with the exception of New Guinea and the Bismarck Archipelago, which were affected during the fifth pandemic. The world distribution of cholera from 1800 to 1945 can be seen from Fig. 1.

FIG. 1. WORLD DISTRIBUTION OF CHOLERA, 1800-1945



= *areas affected by cholera during the period 1879-1911*

The dates indicate the last year in which cholera occurred during the period 1800-1945.

Cholera since 1923

As remarked above, Europe has remained free from cholera since 1923. In fact there has been no westward spread of cholera beyond Afghanistan, apart from sporadic outbreaks in Iran (1927, 1931 and 1938-39) and Syria (1947-48) and a serious epidemic in Egypt in 1947 which caused more than 20 000 deaths in a period of three months. Unlike earlier epidemics in Egypt, this outbreak was not initiated by pilgrims returning from Mecca, since it began in September, before the pilgrims returned. Though various possibilities were suggested, the origin of the epidemic could not be satisfactorily traced. The first

FIG. 2. YEARS OF CHOLERA EPIDEMICS IN THE SOUTH-EAST ASIA AND WESTERN PACIFIC AREAS, 1923-55

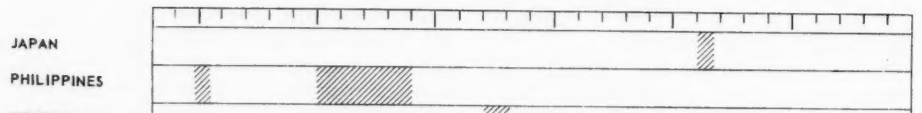
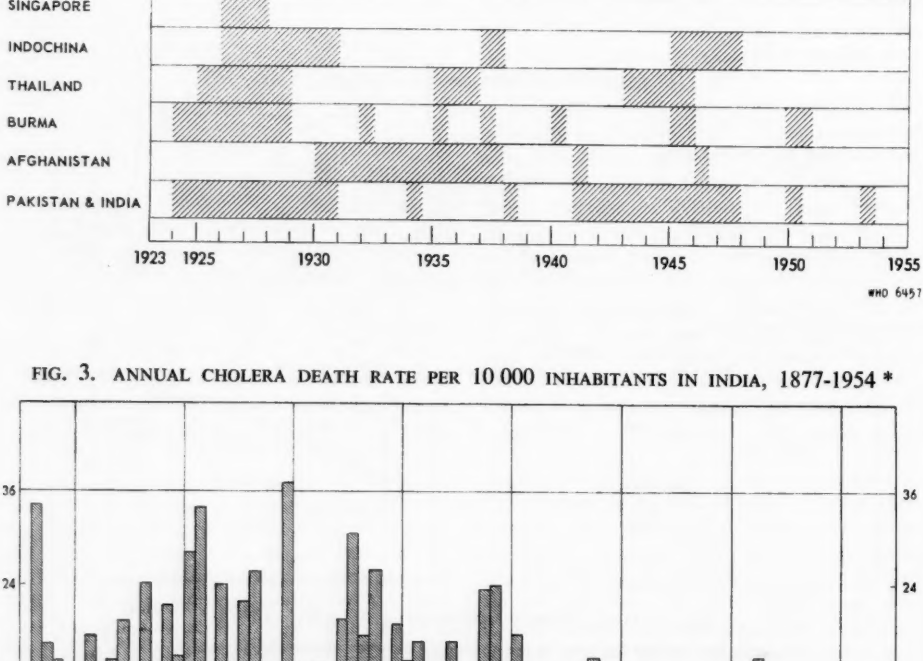


FIG. 3. ANNUAL CHOLERA DEATH RATE PER 10 000 INHABITANTS IN INDIA, 1877-1954 *



** For purposes of comparison, the cholera deaths reported in Pakistan after the partition year of 1947 are included.*

cases occurred at the important trading centre of El Korein in the Delta Province of Sharkiya, where merchants from all over Egypt had congregated to attend the annual date fair. The infection spread rapidly, and within two weeks all the Delta provinces except Beheira were affected, as well as the governorates of Cairo, Damietta and the Canal, and the province of Giza in Upper Egypt. The epidemic continued to extend, reaching its greatest height during the fifth week. It then declined steadily, and by December cholera had practically disappeared from Egypt.

This epidemic in Egypt occurred at a time when the newly constituted Interim Commission of WHO was about to undertake initial preparations for revising, unifying and strengthening existing international sanitary regulations. It provided the Commission with a unique opportunity for testing the effectiveness of these measures. The Commission co-operated closely with the Egyptian health authorities and kept other countries, particularly those closely in contact with Egypt, regularly informed of the epidemiological situation. It also undertook the bulk ordering of cholera vaccines and other supplies from various sources and supervised the application of the International Sanitary Conventions, the provisions of which were found to be adequate; many countries, in fact, had to be discouraged from taking unnecessarily drastic action, in excess of these provisions.

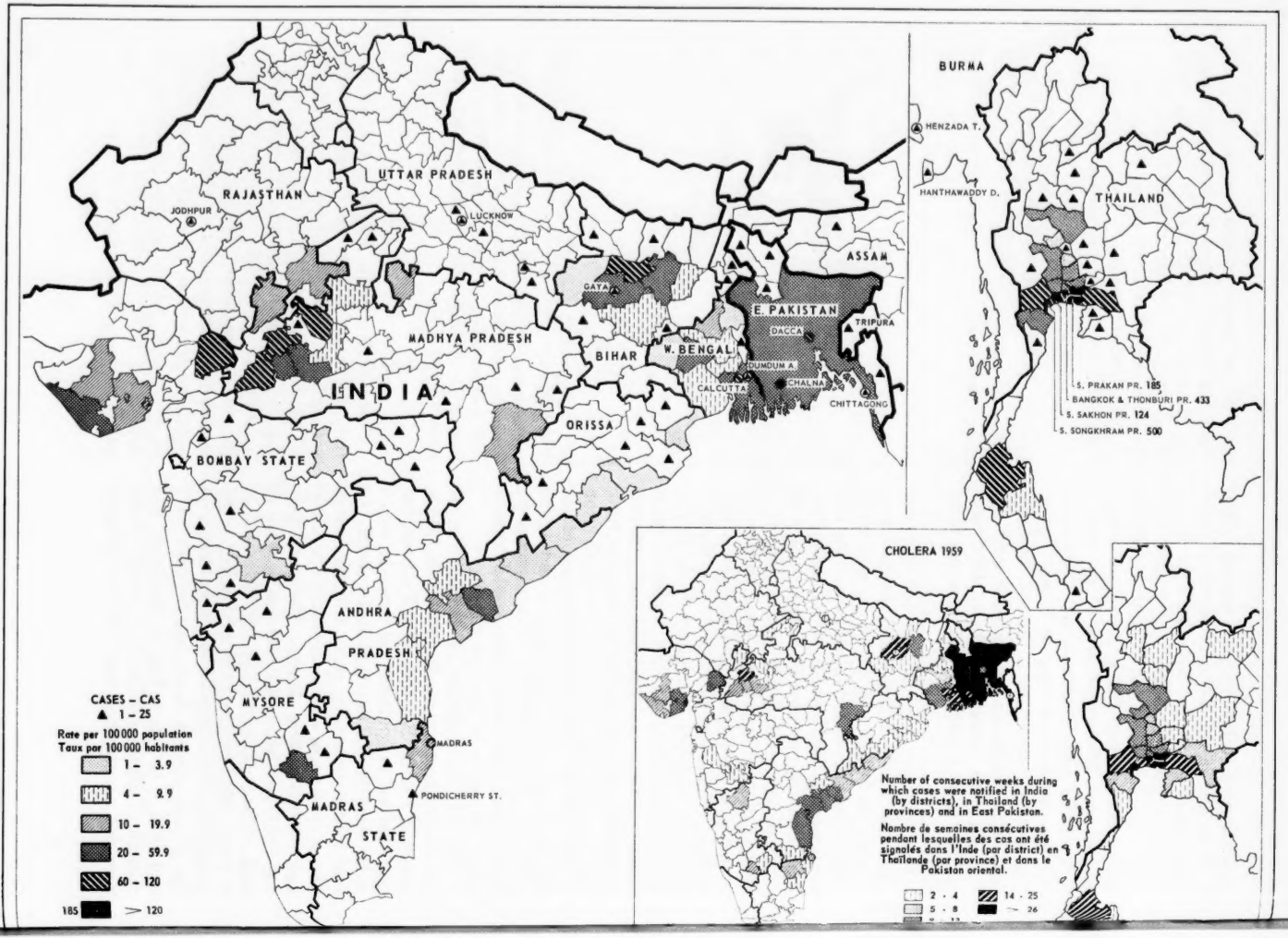
The pattern of cholera epidemics in other non-European countries from 1923 to 1955 is shown in Fig. 2. For India and Pakistan, the years shown as epidemic are those in which more than 100 000 deaths were recorded, but even in the intervening years, with the exception of 1954, there were always between 50 000 and 100 000 cholera deaths. The worst year was 1943, with nearly 460 000 deaths, while in each of the years from 1927 to 1930, as well as in 1924, 1944 and 1945, the total of deaths approached or exceeded 300 000. The decline in the annual cholera death rate between 1877 and 1954 is shown in Fig. 3. Incidence and mortality varied considerably, however, from province to province and even in different parts of the same province; as can be seen from Fig. 4, the highest average endemicity for the period 1901-45 was in the province of Bengal at the mouth of the Ganges delta, and this area has been called " the major endemic home of cholera ". There are marked seasonal fluctuations in incidence.

FIG. 4. CHOLERA ENDEMICITY LEVEL IN INDIA, 1901-45

The endemicity level is shown in relation to the river system by the variation in the density of the dots. This level is expressed by the average annual cholera death rate during the fifteen years of lowest incidence in the period 1901-45.

Since 1955, cholera has been confined to India, Pakistan, Nepal, Burma and Thailand, with small outbreaks in Cambodia and Afghanistan. The situation for 1959 is shown in Fig. 5. The gradual retreat of cholera, first from the west and more recently from countries to the east of the Indian peninsula, is due to complex causes, but undoubtedly vigorous public health action, especially the provision of wholesome water supplies and stringent application of the International Sanitary Regulations, has played a major role.

FIG. 5. THE CHOLERA SITUATION IN 1959



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MALARIA ERADICATION IN AFRICA

In 1955 a survey of malaria in the Chronicle described the malaria situation in tropical Africa as not "quite so promising, owing to the current high cost of malaria control in that region and to the absence thus far of any convincing success on a country-wide scale. There is no reason to doubt that the difficulties will be overcome but one cannot yet foresee the elimination of malaria from Africa in the near future." [1] *Another survey four years later found the prospects somewhat brighter, but residual insecticides alone had not as yet succeeded in bringing about interruption in the transmission of the disease. "The reasons for this may be sought in the epidemiology of malaria in the area, the habits of the main vector,* A. gambiae, *the characteristics of the residual insecticides, the development of resistance... incomplete coverage of the area, the mobility of the population, the problem of finance, and sociological difficulties."* [2]

The following is an extract from a report on the present situation in Africa, prepared recently by Dr M. A. C. Dowling, Senior Malaria Adviser, WHO African Region.

As in most other parts of the world, malaria control in Africa before the Second World War was restricted to the protection of townships and industrial enterprises. The methods used were designed either to control larval forms of the vector mosquitos—by such means as contour drainage and larviciding—or directly to protect the individual—by screening, drug prophylaxis, etc. It was not until the possibilities of the new residual insecticides were realized that the first attempts were made to control rural malaria. The success of these imagicidal measures in reducing the incidence of malaria in some parts of Africa was spectacular; by the end of 1950 encouraging results on a large scale had already been obtained in the Union of South Africa, the Mazoe Valley of Southern Rhodesia, the central high plateau of Madagascar, Swaziland and Mauritius. The Malaria Conference in Equatorial Africa, held at Kampala in 1950 [3] under the joint auspices of WHO and the Commission for Technical Co-operation in Africa South of the Sahara drew attention to the need for setting up or extending control projects to demonstrate the effect of imagicidal and other measures in the notoriously difficult conditions prevailing in tropical Africa. As a result, eight projects were started in West Africa in 1952 and 1953 and were extended in 1955 to embrace a total population of more than 3 million. At the Second Malaria Conference held in Lagos at the end of 1955, the results reported suggested the existence of technical difficulties that could not be easily surmounted. The intense transmission of malaria in West Africa, the development of resistance in *Anopheles gambiae* to dieldrin in North Nigeria, the exophilic behaviour of this vector and other difficulties showed that effective malaria control would not be so easy to obtain in tropical rural Africa as had been hoped.

Meanwhile, outside Africa, spraying with residual insecticides had been remarkably successful in many countries, and the new concept of malaria eradication made its appearance. In June 1956, however, after studying the report of the Lagos Conference, a WHO Expert Committee on Malaria expressed considerable doubt about the advisability of including tropical Africa in the eradication programme at this stage, on the ground that, since there had not yet been demonstrations in tropical Africa of any

[1] *Chron. Wld Hlth Org.*, 1955, **9**, 94
[2] *WHO Chronicle*, 1959, **13**, 348
[3] *Wld Hlth Org. techn. Rep. Ser.*, 1951, **38**

wide areas being cleared of malaria by residual spraying, it seemed premature to plan in terms of continent-wide eradication. The problem of finding an effective and economical method of eradicating malaria in tropical Africa had not yet been solved. Pilot projects were being carried out, and these required increased emphasis and assistance, the Committee considered, so that a solution might be obtained as quickly as possible.

Until 1957, the role of WHO in the malaria programme in Africa had been, in rather more than half of the projects in the region, that of adviser to UNICEF-assisted schemes, with little or no direct responsibility for these individual projects, which were staffed and controlled entirely on a national basis. In the second half of 1957, however, with the creation of the Malaria Eradication Special Account (MESA), WHO was able for the first time to offer more concrete assistance, in the shape of international personnel, training, and supplies. The situation was nevertheless confused, as the reports from the field were conflicting and difficult to interpret. A WHO Malaria Eradication Technical Meeting was held in Brazzaville in November 1957, and the whole subject of malaria eradication and its application in tropical African conditions was exhaustively discussed. In the absence of clear-cut data, the meeting was dominated by current views on African malariology. The failure of residual spraying to interrupt transmission was attributed to behaviouristic changes in the vectors, to the effects of sorption on the insecticidal deposit, to *A. gambiae* resistance to dieldrin (by this time reported from many areas in West Africa), to the irritant effect of DDT: in other words, to the technical shortcomings of the imagicidal attack, which rendered it incapable of interrupting a transmission of the intensity encountered in tropical Africa. The principal conclusions of the meeting were therefore:

(*a*) that the pilot projects in tropical Africa should be strengthened in research, and particularly in entomology, with a view to discovering means of interrupting transmission in such difficult local conditions;

(*b*) that, as residual spraying was not sufficient of itself to break transmission, a series of mass chemoprophylaxis experiments on a large scale should be carried out, both alone and in conjunction with spraying, in order to find out the most effective and economical combination for use in the future eradication programme.

With the new MESA funds at its disposal, WHO was enabled greatly to increase its field staff. The field projects became malaria eradication pilot projects, demonstrating ways of interrupting the transmission of the disease in a variety of local conditions.

Eradication was, however, a new concept in Africa, and its implications and requirements were not fully understood. As a result, the majority of projects simply called themselves " eradication " projects, without in any way altering their organization or their methods. This was the situation throughout 1958, during which year increasing numbers of WHO field and advisory staff were appointed to enable a more detailed and independent analysis to be made of current projects. The following year, 1959, was a period of transition, every project being assessed with specific regard to whether it fulfilled the requirements of eradication. The result of this analysis was startling indeed, and was first communicated to the WHO Malaria Eradication Technical Meeting in Brazzaville in November 1959.

Malaria Eradication Technical Meeting (1959)

The aim of malaria control is so to reduce the incidence of the disease that it no longer represents an important public health problem. By this definition, all the malaria projects in West Africa had by 1959 largely succeeded, parasite rates having been reduced to a relatively low level, and infant mortality having fallen markedly. In terms of eradication, however, this preliminary reduction can be considered as the easiest part of the programme. The interruption of transmission in holoendemic conditions demands a very high degree of efficiency, with an organization capable of ensuring total insecticide coverage and of carrying out a continuous evaluation

of the programme. The subsequent stage, that of systematic elimination of the surviving parasites and of any remaining foci of transmission by the detection of cases and systematic treatment, cannot be brought to a successful conclusion by the type of organization that suffices for malaria control. The data supplied to the 1959 meeting in Brazzaville made it clear that the majority of the current projects had not been planned with eradication as the goal: the concept was still one of control, without adequate emphasis on the perfection of detail needed for eradication. In the absence of a geographical reconnaissance of the project area, the spraying programme was incapable of achieving total coverage. There was insufficient staff. The projects were often directed by part-time officers, and were given very little administrative autonomy. The financing was usually too limited, so that the activities and staffing within the project area were dependent on the current financial position, rather than on the direct requirements of the eradication programme. This was attributable largely to inadequate planning, and to local failure to appreciate the needs of a programme that had eradication as its objective. In addition, the projects were often too small, so that the wide-ranging population movements so characteristic of African communities tended to nullify efforts at interrupting transmission. The trials in mass chemoprophylaxis, introduced in many territories as a result of the 1957 meeting in Brazzaville, had failed for the same reasons. Attendance for treatment varied between 60% and 75%—a wholly inadequate proportion for the purposes of eradication, in which total coverage is an essential of any method employed. Finally, the evaluation staff was too small for a proper interpretation of the results obtained.

The technical difficulties that confront the malariologist in Africa are an important aspect of the malaria problem in that continent. The intensity of transmission by a vector as efficient as *A. gambiae* is such as to demand concentrated effort if eradication is to be achieved. It is important to realize that these technical problems do not prevent eradication in tropical Africa; they do, however, make it more difficult. This was the principal conclusion of the Brazzaville meeting in 1959, at which, for the first time, a representative body of malariologists from all over Africa could state that " if the administrative and financial difficulties could be overcome, malaria eradication should be technically feasible in the African region ". The meeting underlined the need for further study of some of the technical problems with a direct bearing on the conduct of the malaria eradication programme. These include symptomless parasite carriers, the value of fever as a criterion of case detection in immune Africans, the longevity of African *Plasmodium falciparum* in the human host in the absence of fresh transmission, the establishment of an effective single-dose treatment for immigrants entering protected areas, and a variety of entomological problems. The solving of these problems will greatly assist the malariologist in his work by improving the technical weapons at this disposal.

But even the most technically perfect programme will fail to achieve eradication unless it rests upon a sound financial and administrative basis. The meeting made a number of important suggestions about this. Complete preparation and planning are required to ensure a more realistic approach to the many difficulties an eradication programme must face under African conditions. Geographical reconnaissance should be an integral part of each programme, and should be carried out in current projects even if it entails calling a temporary halt to current activities.

The meeting considered that no evidence had been adduced to show that the imagicidal attack had failed in Africa. There are so many recognized flaws in the organization and execution of many of the projects that the effect of residual spraying cannot yet be assessed. In those projects, moreover, in which reorganization has led to total insecticide coverage, transmission has been interrupted. There is a serious shortage of trained personnel at all levels, and particularly of spray supervisors and laboratory technicians.

Finally, the meeting underlined the acute shortage of funds available for eradication in

Africa. Even in ideal conditions, eradication is an expensive procedure, justified only by its ultimate objective. In tropical Africa, however, communications are extremely difficult and the cost to be borne by governments is thus enormously increased. The meeting considered, however, that, although lack of funds might prevent an immediate expansion of the eradication programme to embrace the whole continent, it should not deter governments from preparing themselves, with the assistance of the international organizations, for eradication; for " it is possible that in a number of years' time when global eradication is far advanced, adequate funds will be made available to enable the African projects to be pushed forward to eradication of malaria. By this time, there must be a sufficient cadre of well-trained national personnel at all levels, and the technical problems associated with the interruption of transmission in African conditions must have been solved. "

Implications of malaria eradication in Africa

Certain preliminary questions must be asked in any study of malaria eradication in tropical Africa:

(*a*) Is eradication necessary in tropical Africa, and, if so, is it technically feasible?

(*b*) What organization will be required?

(*c*) How much will it cost?

(*d*) To what extent are African territories ready to undertake eradication?

The most characteristic feature of African holoendemic malaria is the remarkable degree of immunity developed by the individual at a very early age. Even in conditions of intense transmission, the adult African appears to exist in perfect harmony with the parasite, so that the disease exerts no evident ill effects on him. In such circumstances the only apparent toll taken by the disease is in early childhood, which is characterized by a high infant mortality and slow development up to the age of 3 or 4 years. There is a considerable body of opinion [4] to the effect that this immunity, which protects the older child and the adult completely, should not be broken by malaria control measures, except in direct association with economic development. This view has had a considerable deterrent effect on rural control projects in the past, and even at the Brazzaville meeting in 1959 the question of the advisability of eradication in tropical Africa was approached with caution. The immunity has been considered to be of such degree as to relegate malaria to a secondary place in any priority for public health development schemes. There are, however, two important factors that now weigh strongly against this viewpoint. The first is that malaria eradication is a global strategy that must involve Africa if it is to succeed. With the great increase in and ease of international travel, the dangers of reintroduction of the disease into other continents from such a prolific source as tropical Africa must demand an indefinite prolongation of the maintenance phase in countries that have achieved eradication, thus defeating the whole object of eradication. The second factor is associated with the vast political changes in the continent, which have resulted in the appearance of many newly independent countries bent on the economic development and utilization of their own resources. In these countries the existence of malaria is a serious bar to progress, with its effect on children, on general morbidity, and on standards of living in highly endemic areas. In addition, the widespread organization required by the eradication programme, touching as it does every aspect of the life of the population, will help later to form the basis for an expansion of public health activities into other fields.

The doubt as to the advisability, or indeed the necessity, of eradicating malaria from tropical Africa has been associated with widespread scepticism about its technical feasibility. Until recently, the sceptic has been confirmed in his views, for the pilot projects in West Africa have failed to interrupt transmission. When field studies had demonstrated, however, that the reasons for these failures were other than technical, a number of projects were entirely revised, with emphasis on better planning and organiza-

[4] See *Wld Hlth Org. techn. Rep. Ser.*, 1951, 38.

tion. As a result, two examples of presumably interrupted transmission were reported to the 1959 meeting at Brazzaville, in areas, Liberia and Cameroun, where failures had previously been recorded. During 1960, the results from both these projects have continued to improve, which has justified the optimism expressed by the meeting on the technical feasibility of eradication. This does not mean to say that, in a continent-wide programme, there will be no areas refractory to imagicidal attack. It is certain that, as in other parts of the world, there will be areas where additional or alternative measures will be needed to achieve malaria eradication. But the nature and extent of these difficulties will only be appreciated when a large-scale programme with total coverage is established. There is no reason to suppose that the intelligent application of the appropriate measures will fail to eliminate these foci of persisting transmission, whether their cause be technical (vector exophily, insecticide resistance, immigrant parasite carriers, etc.) or administrative in the wider sense (physical difficulty of coverage in swamp or forest areas, localized failures in organization, etc.). Success in these circumstances depends upon the quality of the evaluation services, which must be able to draw early attention to these continuing foci and at the same time indicate the cause of failure, so that the appropriate remedy can be applied.

The organization of malaria projects in Africa has always in the past been geared to the needs of control. The senior staff has frequently been engaged part-time on the project, and a fluctuating budget has precluded the formation of a sound organization. With the change to the concept of eradication, an attempt has been made to adapt these control staffs as they are to the far more stringent new requirements. Lack of appreciation of the needs of eradication has usually resulted in an underestimate of the staff required. Apart from the senior technical staff of doctors, engineers, and entomologists, emphasis must be placed on two vital categories of staff. In the absence of any reliable and simple field test for spraying quality, total coverage can only be ensured by an adequate cadre of supervisors. In many parts of tropical Africa, villages and hamlets are only reached after days of tramping through swamp and jungle. Only a supervisory staff with a true sense of devotion to their work can carry out such difficult duties in an efficient manner, and without total coverage the programme must fail. The second essential category is the staff of laboratory technicians, on whom the whole evaluation of progress depends. The process of case detection relies completely on accurate and rapid diagnosis of blood slides; no easy matter when positive slides are rare and of very low parasite intensity. A missed case may rapidly give rise to a focus of fresh transmission during the consolidation phase, perhaps with serious consequences.

The staffing of an eradication programme does not concern only the technical personnel. All the administrative aspects must receive equal attention, because the smooth development of the whole programme depends on them. The effective running, maintenance and repair of vehicles and spraying machines, the timely delivery of necessary supplies and equipment to the field staff, a clear appreciation of the needs of the programme with realistic budgeting well in advance—all demand the services of a trained staff with clearly defined responsibilities.

Experience elsewhere in the world has shown that a malaria eradication service must have a considerable degree of autonomy within the health ministry, with authority to engage or dismiss personnel. This service must be national in character, although international staff may act as advisers on certain aspects of the work. In order to achieve its objective, the eradication programme must be staffed by personnel who are reliable and devoted to their work, from whom a greater and more sustained effort is demanded than in a simple control scheme. It is evident, therefore, that they must have security of employment and receive salaries commensurate with their responsibilities. In many countries this is appreciated, with a resulting marked improvement in efficiency, and therefore a reduction in expenditure by the speedier attainment of the consolidation and mainte-

nance phases. In some countries, a central co-ordinating board has been set up at ministry level to ensure that there is close co-operation between all departments of government concerned with the eradication programme, such as finance, health, public works, transport, legal and customs revenue. In short, the organization of a malaria eradication campaign is no simple matter, and requires a great deal of preparation and training. Experience elsewhere has clearly shown that no country should embark on a full-scale programme within its borders until it has understood all the implications and requirements of eradication, and is fully prepared in every respect to undertake it. This has a very important bearing on the planning and conduct of the overall programme in the African Region.

It is evident that such a programme will be expensive, but the outlay is justified by the objective, which entails an eventual saving of funds as against the indefinite commitment of control.

Allowing for a maximum period of 9 years, to include preparatory, attack and consolidation phases, a generous estimate of the total average cost of the eradication programme in the African Region is US$6.00 per head of the population, varying between $2.25 and $9.60 at the extremes. A comparison between this figure and that willingly expended for construction of a hotel, a hospital, or, more strikingly, a road or railway, will show that this figure is not an unreasonable one for the economic advantages gained.

Given the elaboration of the organization and the cost of the programme, it will be readily understood that only a comparatively small number of African territories can be considered to be prepared for eradication. The difficulties are aggravated by the fact that the frontiers of the majority of newly independent territories bear little or no relation to tribal or topographical boundaries. Many countries consist of a variety of widely differing zones closely related to similar zones in neighbouring territories but which do not lend themselves to the establishment of programmes within the country. The concept of the country-wide scheme is universally accepted as an essential of eradication, but cannot be applied in much of tropical Africa, where large programmes involving parts of adjoining territories in generally similar areas offer the best chance of success. Such large areas, on a long-term basis, could eventually be merged.

The eradication of malaria from Africa, it may be concluded, is technically feasible. It can be achieved if African countries combine their resources to make a concerted attack on the disease. International assistance will be necessary, and the campaign must be planned with strict regard to the requirements of an eradication programme and in disregard of national frontiers.

Leprosy control

" *International Work in Leprosy* 1948-1959 * is an admirable review of the advances that have taken place in the field of leprosy during the last decade. It is a reprint of an article published in the *WHO Chronicle*, and should be studied by all concerned with the care of patients with leprosy. "

The Practitioner, 1960, **185**, 584

* *International Work in Leprosy* 1948-1959. World Health Organization, Geneva, Switzerland, 1960, 39 pages. Price: 1/9, $0.30 or Sw.fr. 1.—.

ANTIMICROBIAL THERAPY OF TUBERCULOSIS

It is now some fifteen years since the treatment of tuberculosis with streptomycin and PAS (p-aminosalicylic acid) began, and nine years since the highly specific antituberculous effect of isoniazid was discovered. These developments have revolutionized the treatment of tuberculosis by making it a "manageable" disease. In a recent number of the WHO Bulletin, Dr Walsh McDermott, Livingston Farrand Professor of Public Health, Cornell University Medical College, New York, considers the present situation of tuberculosis chemotherapy.[1] *Some of his conclusions are summarized below.*

Experience with the new antituberculous drugs shows that there may come a time when most tuberculous patients will be treated at home. This would solve an important public health problem in regions where the number of patients is considerably greater than the number of hospital beds available for them.

Hospital versus domiciliary treatment

While many patients can now be treated at home, it is held that it is preferable for some to be treated in hospital, particularly initially, since they are then isolated from their immediate household associates, who are liable to be infected, and the rest in bed is allegedly beneficial. However, two recent investigations—one by Hirsch et al.[2] at the Rockefeller Center, New York, and the other by the Tuberculosis Chemotherapy Centre, Madras, India (under the auspices of WHO, the Indian Council of Medical Research, the Government of the State of Madras and the Medical Research Council of Great Britain) [3]—suggest that bed rest is not as important as is usually believed as long as the patient is receiving carefully managed chemotherapy.

As for the other argument in favour of hospitalization, the isolation of infectious cases is still to be regarded as desirable, but it is often not carried out even in the most developed countries; it is difficult, for example, to persuade asymptomatic patients that they can transmit bacilli and should therefore be isolated. When the patient is highly infectious—when the larynx is involved, for instance—it is generally held that he should be kept in hospital, if possible until he is no longer infectious. But the patient who is bacteriologically positive and whose state is such that he would have to be kept in hospital to the end of his life—the patient with a chronic cavitary lesion, to take an example—should be allowed to remain at home if this does not represent too great a risk for his household associates.

When patients are treated exclusively at home, three to six months must be allowed in most cases before the bacilli disappear from the sputum. In practice, therefore, there is little danger for contacts of a case treated at home from the start, for, on the one hand, treatment rapidly decreases his infectiousness, and, on the other, his household associates can be kept under observation and protected.

Choice of chemotherapy for previously untreated patients

The most suitable drugs or combinations of drugs for patients, both in hospital and at home, are, in order of effectiveness:

- — isoniazid with streptomycin daily;
- — isoniazid with PAS daily;
- — isoniazid alone;
- — isoniazid with streptomycin injections two or three times weekly.

[1] McDermott, W. (1960) *Bull. Wld Hlth Org.*, 23, 427
[2] Hirsch, J. G. et al. (1957) *Amer. Rev. Tuberc.*, 75, 359
[3] See *WHO Chronicle*, 1959, 13, 400; 1960, 14, 280.

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There is also another combination of drugs, pyrazinamide and isoniazid, which is probably the most effective against the tubercle bacillus, but is much too toxic for general use, because of the pyrazinamide.

It is generally agreed that, if circumstances are favourable, it is preferable to employ more than one drug. Whatever the scheme of treatment, isoniazid is acknowledged to be the most active antituberculous drug. The use of streptomycin daily is rarely practicable on an out-patient basis.

Isoniazid resistance is encountered, not only when the drug is used alone, but also when patients are receiving PAS at the same time. PAS is most needed when the tuberculous cavities in the lung are more than 2 cm in diameter. Since the major part of the incapacitating action of antituberculous drugs against the tubercle bacillus probably takes place during the first weeks of treatment, it would seem preferable to begin with a combination of drugs—isoniazid-streptomycin or isoniazid-PAS—and to continue with isoniazid alone when the cavity has closed and the patient is no longer infectious.

Administration of isoniazid alone is still of value for prophylaxis and as treatment for tuberculosis without cavitation. It may be employed initially for cavitary pulmonary tuberculosis in special circumstances, e.g., in tuberculosis programmes where the use of PAS would involve additional expense and so restrict their scope, or when PAS is poorly tolerated and daily administration of streptomycin is not a feasible alternative.

If a patient with moderately or far advanced pulmonary tuberculosis is treated with any of the four alternative drugs or combinations of drugs listed above, the course of the disease follows one of three patterns:

(*a*) in most cases there is a considerable regression in infiltration, with closure of the cavities and disappearance of infectiousness;

(*b*) in perhaps 15-20% of cases there is an extensive regression of infiltration, but the cavities fail to close; nevertheless, infectiousness disappears, giving rise to the so-called " open negative " syndrome;

(*c*) in about 15% of cases there is a greater or lesser regression of infiltration, but no considerable reduction in cavity size, and tubercle bacilli continue to be discharged in the sputum. If this happens, the treatment has failed.

Management of cases when chemotherapy has been unsatisfactory

Failure to respond to chemotherapy usually becomes obvious by the end of six months of treatment. The development of resistance by the bacilli may be a result as well as a cause of persistent cavitation, for the walls of the cavity form an excellent medium for multiplication of the bacilli, thus favouring the appearance of resistant strains. Other drugs are available to deal with this situation but unfortunately, because of their toxicity, they can be administered only for some three or four months. Thus it might become advisable to carry out collapse therapy or excision; in any event hospitalization is highly desirable. Whatever new drugs are given, the continued administration of isoniazid has been found worth while, even though *in vitro* resistance to it has been shown to occur.

The other drugs that might be used in these resistant cases are: cycloserine, pyrazinamide, α-ethyl-thioamide, and viomycin.

Cycloserine, administered in a dose of 250 mg twice daily, is very effective in combination with isoniazid. It may, however, cause epileptiform seizures, and, as the margin of safety is low, it is preferable to reserve it for hospital use. Pyridoxine is said to neutralize the neurotoxicity of cycloserine, but it is not known whether it also decreases its efficacy against the tubercle bacillus.

Alpha-ethyl-thioamide is effective and has given good results with isoniazid, but it causes severe nausea and vomiting, and there is also some evidence of a cumulative effect with isoniazid in the production of peripheral neuritis. The combination of α-ethyl-thioamide with cycloserine might be quite an effective short-term treatment if the patient tolerates the drugs.

Pyrazinamide is of only limited value alone, but is very effective in association with iso-

niazid and provides perhaps the best combination. Its toxicity must be borne in mind, since it causes hepatitis with jaundice in about 3% of patients, with a fatal outcome in about one third of those who develop jaundice; consequently its use is restricted to cases where the danger from the disease exceeds that from the toxicity of the drug. Mention should be made of the effectiveness of pyrazinamide in combination with streptomycin. As a result of one study it was held that this combination of drugs should be given to patients with advanced cavitary disease as primary treatment, and to most patients with pulmonary tuberculosis who had failed to respond to isoniazid with PAS.

These secondary drugs should, in general, be prescribed only when treatment has clearly failed, and not merely because bacilli cultured from the patient's sputum are resistant to isoniazid *in vitro*. Needless to say, they can be given only in hospital.

A standard form of treatment for pulmonary tuberculosis might be as follows: isoniazid-PAS daily during six months, or at least until there is clear evidence of therapeutic failure. Then, if there is failure, excision or collapse therapy with administration of streptomycin plus cycloserine, α-ethylthioamide or pyrazinamide, in that order of preference, in addition to isoniazid. What of the patient severely ill with extensive acute tuberculous pneumonia? Here isoniazid plus daily streptomycin should be given until there is an improvement and infectiousness disappears; this treatment calls for four to eight months' hospitalization. Subsequently, isoniazid alone may be prescribed, provided that there are no cavities of 2 cm or more in diameter. If streptomycin has already been given for three or four months before therapeutic failure becomes clear, the best procedure is to employ two of the three secondary drugs together for as long as possible, bearing in mind their toxicity.

The toxicity of *viomycin* prevents its use except for serious forms of the disease, e.g., laryngeal tuberculosis, and then only for a limited period and in very special circumstances. It may cause deafness and nephritis. *Neomycin* is too toxic systemically and is used only locally; so too is *kanamycin*, which also causes deafness. The use of these last two drugs is not advisable.

Treatment of patients with the "open negative" syndrome

This treatment is difficult to standardize, for each case must be considered on its merits, as in the majority of cases the disease must still be regarded as active. Surgery might be advisable in some cases—say, in a young physician or dentist, even though his sputum continues to be non-infectious with continued treatment. In the case of middle-aged or older patients or those without much contact with young subjects, chemotherapy might well suffice.

Duration and dosage of chemotherapy

In pulmonary tuberculosis it has become common practice to continue treatment for 18-24 months, but it is probable that the principal therapeutic action occurs during the early weeks, the drugs exerting only a protective or suppressive action thereafter. In most cases, it is wise to continue chemotherapy till well past the period during which most of the healing takes place.

Streptomycin should be given at the rate of 20 mg/kg body-weight per day, i.e., an average of 1 g per average-size adult. More may be given, say, 30 or 40 mg/kg per day during short periods of two or three weeks, but there is a considerable risk of vestibular damage, especially in older age groups. When given with streptomycin, as much as 20 g of PAS per day may be necessary. With isoniazid, the PAS dose depends on the isoniazid dose; for example, it seems suitable to give 6 to 10 g per day when the daily dose of isoniazid is 300 mg or more. The ideal dosage of isoniazid is the highest tolerated; this for most people lies between 5 and 8 mg/kg per day. While the latter dose approaches the toxic range, it can be given in certain cases over a period of several weeks. Toxicity is manifested by the appearance of peripheral neuritis and encephalopathy, in the form of epileptiform seizures. For prefer-

ence, therefore, the dose of isoniazid should be 300-450 mg per day, depending to some extent on the patient's size.

The appearance of drug-resistant tubercle bacilli must be taken into consideration in the treatment of a patient who persistently excretes bacilli in the sputum after three or four months of isoniazid therapy.

At present, no laboratory tests are available, apart from bacteriological examination of the sputum or gastric fluid, that will give the information required for a rational initial choice of, or a change in, chemotherapy. If the patient has not yet received treatment there is a very good chance that the bacilli will be susceptible to isoniazid, and after six to nine months' treatment there will be no more danger of resistance to this drug than to others. Resistance may finally appear, however, although its occurrence to a significant degree is less frequent than is generally thought. Hence, if the improvement in the X-rays is not sufficient and if bacteriological tests are positive after five or six months of isoniazid treatment, it is advisable to change the treatment and also to consider collapse therapy or excision. On the other hand, if, after five or six months of isoniazid treatment, the patient shows sufficient X-ray improvement, including absence of cavitation, and the bacteriological tests are negative, the clinician may rest assured that isoniazid treatment will almost certainly retain its effectiveness in the future and that significantly resistant strains will not appear.

The " open negative " syndrome poses a special problem in short-term treatment, and from the long-term viewpoint no prognosis can be made.

Epidemiology

The essential point that must be remembered in connexion with epidemiology is that isoniazid-resistant bacilli infecting new subjects will probably cause a tuberculous infection that will itself be isoniazid-resistant. However, we are without reliable information on this point and must fall back on our general knowledge of the epidemiology of tuberculosis. It must be borne in mind that only a small number of those who develop tuberculous infection subsequently develop tuberculous disease.

It may also be taken that, since the introduction of isoniazid, far more people have died because they did not receive the drug than have been seriously affected by isoniazid-resistant tubercle bacilli.

Importance of collapse therapy

It is regrettable that pneumothorax has been virtually abandoned, for, since the persistence of cavities promotes bacillary resistance, anything that will help to eliminate them should be undertaken to prevent resistance from developing. For various reasons, it is not always desirable to remove the lesions surgically, and such operations are seldom indicated during the early months of antimicrobial therapy. Hence it does not seem desirable to abandon the practice of pneumothorax, especially as it would appear that there is no reason nowadays to fear most of the serious complications that used to attend this procedure in the past. It could be carried out, in conjunction with chemotherapy, in many patients with cavities 2-4 cm in diameter and extensive pulmonary infiltration.

In this way, unsuccessful treatment might often be avoided, e.g., in cases in which cavities remain open, giving rise to problems of resistance and therapeutic failure. Pneumothorax would be a highly satisfactory adjunct to chemotherapy in patients difficult to hospitalize or who, when hospitalization is possible, cannot undergo operation, for it lends itself well to ambulatory treatment, requires only periodic supervision of the patients, and permits reasonable physical activity on their part.

LABORATORY RESEARCH ON THE POLIOMYELITIS VIRUS

Among the subjects of research reviewed in the proceedings of the Second International Conference on Live Poliovirus Vaccines [1] were poliovirus "markers" and simian viruses. The following summary of papers and discussions on these subjects published in the proceedings may give some idea of the intricacy of the problems that must be solved to ensure, in an objective and verifiable way, that live poliovirus vaccine is harmless and effective.

"Marker" characters of viruses

What happens to polioviruses ingested during vaccination when they multiply in the alimentary tract? Do they remain unchanged, or does their progeny differ from the original strain? Do some of their characters change, mutations bringing about a return of the original neuropathogenicity? Are the viruses genetically stable or not? These questions are of fundamental importance, for one of the great unknowns of oral poliomyelitis vaccination is the fate of the viruses, attenuated when they are administered but then released into the community and thereafter free from all control. When poliomyelitis occurs in someone who has been vaccinated, and it becomes important to ascertain the relationship between the pathogenic virus and the vaccine virus, how can the one be distinguished from the other?

The experiments, studies and researches that have been going on for the last ten years have been conducted with the utmost caution, for, as Koprowski, one of the pioneers in the field, pointed out at the Second International Conference on Live Poliovirus Vaccines:

"The requirement that a product remain absolutely stable after passing through the alimentary canal can be applied to magnesium sulfate or other chemical laxatives, but not to a self-multiplying agent such as poliovirus." (page 7)

There must consequently be methods of investigation that will enable morphologically identical viruses to be distinguished. Research workers have been seeking by tissue cultures—particularly on the kidney tissue of monkeys—the differences that would serve as "markers" and enable a distinction to be made. Two groups of methods have been proposed. One group is serological, using very sensitive techniques to identify strains of the same type of poliovirus through neutralization of the virus antigens by the corresponding antisera.[2]

Another group of methods relies on cultural or physico-biochemical characters, called "marker" characters. Much hope has been placed in these methods, for it was thought that a relationship could be established between some of these characters and monkey neurovirulence, which in turn was thought to be closely related to the neuroparalytic effect of the virus on man. Such a correlation would have had the great practical advantage of justifying the substitution of laboratory tissue culture tests for lengthy and expensive tests in monkeys. The main characters are as follows:

1. The ability to develop in tissue culture at 40-41°C. (T+ or T−). The association of the T+ character with neurovirulence has occurred regularly enough in numerous studies to justify the belief that there is a definite relationship between these two characters. They are considered to be genetically very close.

2. The capacity to develop at a certain pH under agar of low bicarbonate content (d+ or d−).

[1] Second International Conference on Live Poliovirus Vaccines (1960) *Live poliovirus vaccines. Papers presented and discussions held at the . . .*, Washington, D.C., Pan American Sanitary Bureau, Regional Office for the Americas of the World Health Organization. See also page 35 of this issue of the Chronicle.

[2] See *Bull. Wld Hlth Org.*, 1960, 22, 235.

3. The appearance of the plaques (cytopathic change) in tissue cultures of fresh monkey kidney and established lines of monkey kidney (MS+ or MS−).

Recently an additional physico-chemical technique was proposed: adsorption and elution of virus on a column of ion-exchanging cellulose resin, indicative of the different avidity of the cellulose resin for virulent and attenuated strains. This method requires further study.

The value of these markers is undeniable, and the search for others is continuing in the hope of providing a sounder basis for this type of investigation. For at the moment opinion is far from being unanimous on the respective importance of the various markers. Their correlation with pathogenicity for man and neurovirulence for the monkey is apparently not well enough established for tests on animals to be dispensed with. Individual variation and mutation in these characters do not make the problem any easier. Some of the participants in the Conference call for prudence in the interpretation of these variations. Thus Cabasso et al. hold that

"... it is important to recognize our ignorance concerning the basic mechanisms involved in neurovirulence and the degree to which these various markers reflect this mechanism. The correlation of these markers with neuroactivity is imperfect, indicating that other and unknown factors also play a role in neurovirulence. This is in all probability to be expected, since the growth of a virus within a cell is dependent not only upon the environmental conditions outside the cell, as pH and temperature, but also upon the presence of proper receptors on the cell surface and perhaps an entire battery of as yet unknown enzymes necessary for initiating and carrying out the complex operation of virus synthesis and release." (page 36)

And later Dulbecco says that:

" One would be inclined to predict that there does exist [in the genetic material of the virus] a special group responsible for neurovirulence ... it is very possible that the neurovirulence is essentially an expression of a surface property of the virus, related to the attachment of the virus to special receptors or special types of cell, namely, the neurons." (page 49)

The nature of virulence later comes under discussion. Stuart-Harris notes that:

"... in comparison with ... last year, this year we have a good deal more information concerning the properties of the strains used as vaccines and also of the properties of the strains recovered from children immunized with vaccines. All of this information seems to me to point in the same direction, namely, that whatever property particular we study in relation to these strains, we come up with something which can only be described as a graded characteristic... One did not just have virulent strains or non-virulent strains; one had a spectrum of this particular property." (page 109)

And Dulbecco adds:

" Actually, probably for every mutant listed there, we found a number of different steps so that there are many intermediate degrees of expressions of the same characters, and not simply a few well-defined types ... [This] is a fact which very greatly disturbs the worker with the mutants and also hampers the interpretation of the facts." (page 110)

Simian virus

Monkeys kept in laboratory colonies frequently harbour viruses, some of which are pathogenic to man and have already caused fatal accidents. By hygienic and quarantine measures transmission of the viruses from one monkey to another has been prevented and monkeys to be used for tests with poliovirus have been cleared of the viruses, but the problem is far from being solved.

Since monkey kidney tissue has come into common use for virological research, several dozen new simian viruses have been discovered, which manifest themselves by spontaneous cytopathic lesions in tissues intended for the culture of other—and especially poliomyelitis—viruses. These viruses may, because they develop more slowly than polioviruses, pass unobserved and yet be undesirable contaminants—although some research workers minimize this drawback, pointing to the omnipresence of viruses and to the appearance, recognized or not, of adventitious viruses in biological preparations or our daily bread that do not appear to have any pathogenic effect on man.

The simian viruses of kidney tissue cultures described up to recently had a cytopathic effect which led to their discovery. Recently, however, there has been discovered a " non-detectable " virus or " vacuolating agent ", so called because of the vacuolation of the cells it infects. This vacuolation occurs only in the kidney-cell cultures of the African green monkey; in kidney cells of other monkeys such as *Cynomolgus* and *Rhesus*, much used for virological research, the virus is a silent, "non-detectable" contaminant. Its presence can actually be detected by serological methods and by transferring cellular material to green-monkey kidney tissue, where it proliferates and produces the typical vacuolations. This virus, which may be a silent associate of poliovirus in cultures, does not produce any specific antibodies in man, and may be assumed not to multiply in and therefore to be harmless to him. But its discovery is none the less important. It suggests the possible existence of other undetected viruses, of undiscovered contaminations, of hidden sources of error in the assessment of tests on tissue culture. It is not beyond the bounds of possibility that interference phenomena occur between these " non-detectable " viruses and viruses being cultured, or that a hidden antagonism falsifies the results of tests from which the research worker thinks he has eliminated all possible sources of error.

To eliminate any possible danger arising from these " non-detectable " viruses in the preparation of poliomyelitis vaccine, Dulbecco suggested that the vaccine should be purified by chromatography and equilibrium density gradient sedimentation. The latter is particularly suitable for poliovirus, which is probably one of the animal viruses of highest density.

SIMIAN MALARIA

WHO's campaign for the eradication of malaria throughout the world rests upon the premise that there is no animal reservoir in malaria, as there is in other diseases, of sufficient importance to maintain the disease as a constant threat to man once it has been stamped out in human populations. It has recently been discovered that monkey malaria is transmissible to man. This discovery and its implications for the malaria eradication campaign are discussed below.

The knowledge that malaria parasites of monkeys can be transmitted to man dates back to 1932, when it was found by Knowles & Das Gupta in India that *Plasmodium knowlesi* could cause a febrile infection in man. This parasite was even used for some time to induce malaria in the treatment of general paralysis of the insane.

Knowledge of simian malaria in relation to man was extended in 1948, when *P. rodhaini* of African chimpanzees was found to be morphologically and immunologically identical with *P. malariae* of man. Subsequent work showed that human malaria parasites such as *P. vivax*, *P. falciparum* and *P. ovale* could be transmitted to chimpanzees through anopheline mosquitos, although patent parasitaemia appeared only in splenectomized apes.

When a WHO Scientific Group on Malaria Research met in Geneva in November 1959, it was mentioned that in certain parts of West and Central Africa the chimpanzee is known to harbour *P. malariae*, and that man has been shown to be readily susceptible to the strains harboured. The anopheline vector of the *P. malariae* of these chimpanzees has not been identified. In Sarawak certain strains of human parasites of quartan malaria have been observed to have a peculiar morphology which suggested that the parasite might be of simian origin. In the Amazon region of South America some vivax infections in man have been held to be derived

from simian malaria. *P. simium*, found in howler monkeys of the forests near Santos, has been suspected of being closely related to *P. ovale*. The Scientific Group thought that all these were matters on which research should be undertaken but that they did not seem to have any urgent bearing on malaria eradication.

In May 1960 there was a new development. During research at the US National Institutes of Health (NIH), Bethesda, Md., by Eyles, Coatney & Getz,[1] on the transmission to rhesus monkeys of *P. cynomolgi bastianellii*, some very large-scale inoculations of sporozoites into monkeys were carried out. Two staff members of the Institutes, neither of whom had had any recent contact with human malaria, were dealing at close quarters with heavily infected mosquitos; and they both developed illness with fever which, after a remittent period, proved to have a tertian periodicity. Blood smears, made on new slides and stained in clean dishes with new stain, showed that both had vivax-type parasites with enlarged erythrocytes and Schüffner's stippling. Five ml of blood from each of the two individuals, injected intravenously into two uninfected rhesus monkeys, produced cynomolgi-type infections in 8 days in one monkey and in 10 days in the other. Two human volunteers each received 10 ml of blood intravenously from one of the individuals; both developed clinical attacks of malaria with vivax-type parasites, enlarged erythrocytes, and Schüffner's stippling, but without high parasite densities.

The two staff members in whom the infection was first discovered received chloroquine treatment within 24 hours of diagnosis. At the time of treatment both showed low levels of parasitaemia. The parasites promptly disappeared with treatment and no relapse occurred.

Another staff member allowed 30-50 *Anopheles freeborni*, heavily infected with *P. cynomolgi bastianellii*, to feed on him, and experienced headache, malaise and fever 11 and 12 days later. No parasites were found in his blood, but a monkey free of disease, into which 10 ml of his blood was injected intravenously, developed an overt infection in 6 days. A fourth staff member developed a typical malaria paroxysm with vivax-type parasites 14 days after being bitten by 10 *A. freeborni*, heavily infected with *P. cynomolgi bastianellii*.

After Eyles, Coatney & Getz had submitted their report for publication, they received news from Dr Leon Schmidt that one of his staff in the Christ Hospital Institute for Medical Research at Cincinnati had had an attack of malaria after working with typical *P. cynomolgi* and the sub-species *bastianellii*. His blood had produced a typical cynomolgi-type infection in a rhesus monkey.

Cross-immunity studies were undertaken at Bethesda on two monkeys which had recovered spontaneously from infections with *P. cynomolgi bastianellii*. On being reinoculated with heavy doses of parasites taken from one of the two monkeys which had been infected by intravenous injection of the blood of one of the two accidentally infected NIH staff members, one monkey showed a transient parasitaemia indicating almost complete immunity. The other had an attack of malaria that was shorter and less severe than the usual bastianellii attack. These results supported the view that the human infections were undoubtedly due to *P. cynomolgi bastianellii*.

The significance of these infections of human beings lies in the fact that they were transmitted by mosquitos which had fed on rhesus monkeys. The theoretical possibility of natural infection of man with monkey malaria had already been suspected; but it was the anthropoid ape, not the monkey, which used to be suspected of being a possible carrier of human malaria. Monkeys are much more numerous and widespread than apes, and live in closer association with man, and at least seven species of anophelines are known to be able to transmit *P. cynomolgi* to rhesus monkeys. Some of these species are exophilic, and therefore unlikely to be affected by residual insecticides; moreover the host preferences of anopheline vectors for man and for the monkey are often almost the same. Consequently, experimental proof that

[1] Eyles, D. E., Coatney, G. R. & Getz, M. E. (1960) *Science*, **131**, 1812

man can be infected by monkey malaria opens up a new range of possibilities.

What relation, if any, have these discoveries to the WHO campaign for the eradication of malaria throughout the world? Can we still subscribe to the view of the WHO Scientific Group on Malaria Research that simian malaria has little bearing on malaria eradication at present? On the whole, we can. Some of the eradication programmes have progressed more slowly than was at first expected; but it has become clear during the past few years that in the vast majority of cases the success of a malaria eradication campaign carried out on the lines advocated by WHO is directly proportional to the efficiency of total coverage. There is no reason to think that this new discovery will retard the successful progress of malaria eradication in most parts of the world. There are many large tracts of territory where monkeys are few or absent; and where monkeys exist they do not necessarily suffer from types of malaria that could be transmitted to man by the local mosquitos. It may happen exceptionally in some part of some country that the persistence of infective foci of malaria, despite total spray-coverage and efficient surveillance, might in the future be traceable to some association between the monkey, the vector, and the human being. If the association were to be proved (at present it is purely hypothetical), appropriate action would have to be taken, by elimination of the animal reservoir, by using our considerable resources against the vector, or by some other means. On the other hand, we do know that malaria has been eradicated from large areas of Venezuela, despite the presence of large numbers of monkeys.

The whole problem of simian malaria and its possible implications was placed before the WHO Advisory Committee on Medical Research in June 1960, and was a main item in the agenda of the meeting of the WHO Expert Committee on Malaria in July 1960. Dr G. R. Coatney, of the US National Institutes for Health, one of the authors of the report on human *P. cynomolgi* infection mentioned above, was present as a member of the Expert Committee. Dr P. C. C. Garnham, a leading authority on simian malaria, also attended the meeting, as a special consultant for the discussions on this item.

The Expert Committee's view of the new discovery was as follows:

"... In the present state of our knowledge, it seems that malaria, as a zoonosis, is of only limited importance in the global programme of malaria eradication. The areas where foci of human malaria could perhaps be maintained from a simian reservoir of infection are few and relatively small in relation to the enormous territories where monkeys either do not exist or are in very small numbers, or where simian malaria parasites are absent, or non-infective to man, or not transmissible by those *Anopheles* which transmit human malaria.

" The true significance of simian malaria in relation to man will become apparent when the eradication of human malaria is accomplished in such areas of the world as Malaya, Borneo, Indonesia, Philippines, Taiwan, Central and West Africa. It is interesting to note that in large areas of Venezuela, in which malaria eradication has been achieved and which are known to contain large populations of monkeys, no sporadic cases of malaria have arisen, as would have been expected had there been a simian reservoir of malaria. "

Dr Coatney informed the Committee that a research team is to be sent to Malaya by the US National Institutes of Health to carry out: (1) the isolation in the field and the study of new strains of simian malaria parasites; (2) studies on the transmissibility of human strains of malaria parasites, collected in the field, to lower monkeys; (3) a search for the natural vectors of simian malaria; and (4) studies of the malaria of lower and higher monkeys in man. It is believed that the results of these studies will contribute greatly to our knowledge.

Finally, the Committee expressed the opinion that the discovery of the transmission of *P. cynomolgi bastianellii* to man through *Anopheles* is of great importance in chemotherapeutic research, since for the first time a malaria parasite of a higher mammal, easily transmissible to man, can be used for the laboratory trials of drugs that may be of importance in malaria eradication. Far from being a threat to the campaign for the eradication of malaria, therefore, the discovery may be of positive value to it.

EXECUTIVE BOARD: TWENTY-SIXTH SESSION

The Executive Board of WHO met in Geneva for its twenty-sixth session, from 25 October to 5 November 1960, under the Chairmanship of Dr H. M. Penido. The Vice-Chairmen were: Dr A. O. Abu Shamma and Dr V. Butrov. Dr J. Adjei Schandorf and Dr M. Etemadian were Rapporteurs.

Assistance to the Congo (Leopoldville)

Dr M. G. Candau, Director-General of WHO, reporting on the assistance given to the Congo (Leopoldville), stated that in July, at the request of the Secretary General and the Security Council of the United Nations, WHO agreed to take part in the United Nations emergency programme in the Republic of the Congo.

To meet the emergency, the Director-General had immediately assigned 28 staff members to the Congo and appealed to the League of Red Cross Societies and to the International Committee of the Red Cross to recruit emergency medical teams from national Red Cross Societies. Within a few weeks 28 medical teams had been sent by 25 national Red Cross, Red Crescent and Red Lion and Sun Societies. As a result of these measures it had been possible to get a number of hospitals operating again, not only in the big cities but also in the interior.

As the crisis dragged on it became essential to take action to meet long-range needs. As there were no Congolese doctors, *assistants médicaux* were selected for further training so that they might become fully qualified doctors. Several of these were given WHO fellowships to attend schools of medicine in France and they were also provided with tutors to guide them in their studies. They should graduate in three years' time. Fellowships were also awarded to students to attend the Lovanium University, for which WHO provided 9 professors for the medical faculty and 4 for the school of nursing. Meanwhile, the United Nations had guaranteed the funds necessary for WHO to engage 130 health workers of all categories to work for the Congolese Government, and these were being recruited.

Dr Candau concluded by emphasizing that, if political stability and normal administration could be guaranteed, the medical problems would not be difficult to solve: the preventive work carried out under the Belgian administration could then be resumed and the threat of spread of disease effectively averted. In view of the fact that 700 000 Congolese were in their first year of primary education and 21 800 in their first year of secondary education, the future could be faced with greater optimism.

The Board commended the Director-General for the prompt and effective measures taken to provide health assistance to the Republic of the Congo, and asked him to continue to render such assistance with special emphasis on the training of local staff. It also thanked the International Committee of the Red Cross, the League of Red Cross Societies, and the governments which had helped in the emergency health programme.

Programme and budget for 1962

The Board recommended the adoption by the Fourteenth World Health Assembly of an effective working budget of $21 576 480 for 1962. The amount originally proposed by the Director-General for 1962 was $20 852 000, representing an increase of $1 876 646 (9.89%) over the level approved by the Thirteenth World Health Assembly for 1961. This increase provided for an expansion in field activities ($996 320), increased statutory staff costs ($359 890), an expansion in headquarters activities including

medical research ($425 516), and increased requirements for organizational meetings ($79 970) and for regional offices ($14 950).

Following the submission by the Director-General of supplementary estimates for 1961 to the amount of $825 374 to provide *inter alia* for the administrative and operational services costs at headquarters and in regional offices of the malaria eradication programme, and assistance to the Republic of the Congo (Leopoldville), recommended by the Executive Board for approval by the Fourteenth World Health Assembly, the Director-General proposed an increased effective working budget for 1962 of $21 599 380 to provide for the continuing costs of these items, in the total amount of $747 380. The increase proposed by the Director-General for these purposes was endorsed by the Executive Board which, however, recommended reductions amounting to $22 900 in the provisions for certain project activities in the European Region, resulting in its recommending a budget level of $21 576 480. This figure is 8.97% higher than the recommended revised level for 1961 including the supplementary estimates for that year submitted by the Director-General.

In recommending the budget level of $21 576 480 for 1962, the Board noted that the total estimated expenditure from all sources on international health programmes with which WHO would be associated in that year was of the order of $54 600 000. The Board appreciated that some of these programmes were still at a tentative stage and that certain decisions to ensure their financing had still to be taken by the bodies concerned. Nevertheless, in the light of the information available as to the scope of these programmes in 1962, the Board considered that the budget estimates for that year were adequate to enable the Organization to carry out its constitutional functions. The Board considered also that the Organization was well equipped to carry out the programme planned for 1962, a programme which was in conformity with the general programme of work for the period 1962-1965 as approved by the Thirteenth World Health Assembly.

In making its recommendation on the budget level, the Board considered the financial implications for governments, taking into account the available data concerning the present world economic situation ; the extent of the expected financial participation by governments in WHO-assisted projects in their own countries ; the status of collection of annual contributions and of advances to the Working Capital Fund ; and the availability of casual income to help finance the 1962 programme.

The recommendations of the Board concerning the proposed programme and budget for 1962 were adopted by 16 votes to 1, with no abstentions.

Malaria Eradication Special Account

The Director-General presented a report on the status of the Malaria Eradication Special Account as of 30 September 1960. The total amount of the contributions received or pledged by that date was $12 646 300, expenditure up to the end of 1960 being estimated at about $11 662 600. The fund was short of some $4 785 000 required for financing the malaria eradication programme in 1961.

In view of the situation, the Board considered that in principle some part of the programme should be financed from the regular budget of WHO. The Director-General was urged to continue efforts to obtain voluntary contributions, and a plan for the issue by Member States of postage stamps devoted to the programme was endorsed. The Universal Postal Union was invited to co-operate with WHO in this plan which, it was hoped, would encourage interest in the battle against malaria.

During the session of the Board, the Government of the United States announced a contribution of $4 000 000 to the Account for the year 1961, thus bringing the total amount it had donated up to $15 000 000.

Voluntary Fund for Health Promotion

A report was presented on contributions to the various sub-accounts of the Voluntary

Fund for Health Fromotion. These included US Government grants to the Special Account for Medical Research for bilharziasis research and for research on insecticide resistance and vector control. A contribution to the same sub-account has been made by the Swedish National Association against Tuberculosis and Other Social Diseases in the form of annual fellowships for cardiology research, beginning in 1960.

The Government of France has made a contribution to the Special Account for Assistance to the Congo, consisting of the services of four mobile medical teams in the Congo for a period of six months.

Headquarters accommodation

The Director-General submitted a progress report on work on the new WHO building. The contract with the architect had been signed at the end of May, and since June the architect had been revising the plans to take into account the modifications suggested by the jury as well as certain changes in the Organization's requirements. The building site promised by the Canton of Geneva had been placed at the disposal of the Organization and drilling had already started. Negotiations in connexion with the building loans offered by the Swiss Confederation and by the Canton of Geneva were very well advanced. A Standing Committee on Headquarters Accommodation was established by the Board, and expressed its satisfaction with the progress made to date.

Use of Russian as a working language

The Board supported in principle the adoption of Russian as a third working language in the Regional Committee and the Regional Office for Europe. It recommended to the Fourteenth World Health Assembly that it " take measures for a phased introduction of the Russian language as the third working language in the Regional Organization for Europe, and with the view of full implementation of the principle by 1963 ".

Increase in membership of the Executive Board

The Director-General announced that on 25 October 1960 a further Member had accepted the amendments to articles 24 and 25 of the Constitution and that the acceptance by two-thirds of the Members required under article 73 of the Constitution had thus been obtained. These amendments, whereby the membership of the Executive Board is raised from 18 to 24, therefore came into force as of that date.

Darling Foundation Prize

The Board noted the decision of the Darling Foundation Committee to make the seventh award of the Darling Foundation Medal and Prize jointly to Sir Gordon Covell, of the United Kingdom, and Dr Arnoldo Gabaldón, of Venezuela. The presentation of this award, which was established by the League of Nations to honour the work of eminent malariologists, will be made by the President of the Fourteenth World Health Assembly during a plenary meeting of the Assembly.

Regional Director for the Western Pacific

The Board decided to extend the term of office of Dr I. C. Fang, WHO Regional Director for the Western Pacific, for a further five years, i.e., until 30 June 1966. Dr Fang has held his present post since 1951, and this will be his third term of office.

Technical discussions at World Health Assemblies

The Board asked the Director-General to invite Dr Arnold Sauter, Director of Public Health of the Federal Government of Switzerland, to preside at the technical discussions at the Fourteenth World Health Assembly, which will deal with " Recent progress in tuberculosis control ". It was decided that the subject of the technical discussions to be held on the occasion of the Fifteenth World Health Assembly would be " Mental health programmes in public health planning ".

Place and date of next session

The twenty-seventh session of the Executive Board will be held in New Delhi, commencing on 30 January 1961, i.e., immediately before the Fourteenth World Health Assembly which will also be held in New Delhi.

Notes and News

Vaccination against brucellosis in the USSR

Brucellosis is common among sheep and goats in the USSR, particularly where pedigree fine-fleeced sheep are raised. These animals are the source of infection in 85-95% of cases with manifest clinical symptoms both among people engaged in livestock rearing and among the population in contact with sick animals. Transmission of the disease through milk and milk products has been reduced by the introduction of hygienic measures for the processing of dairy products.

In an article to be published shortly in the *Bulletin of the World Health Organization*, P. A. Vershilova[1] describes the extensive action taken in the USSR to eliminate brucellosis among farm animals and to protect human beings by vaccinating them with live vaccine.

Although there has been no decrease in animal infection in a number of districts, vaccination reduced human infection by nearly 60% between 1952 and 1958. The vaccine consists of a bovine strain of *Brucella*, *Br. abortus* 19-BA, a strain from a dissociated colony of a culture of *Br. abortus* 19 that proved more effective than strains of *Br. melitensis* and *Br. suis*. Cross immunity (i.e., non-type-specific immunity) exists between variants of *Brucella*, and the epidemiology seems to show that brucellosis of cattle or pigs immunizes against sheep brucellosis. The level and duration of immunity depend on the intensity of vaccination and the duration of the vaccination infection (which itself is dependent on the residual virulence of the culture and the dose of vaccine). The effective doses by subcutaneous administration should contain 400-600 million viable brucellae. The frozen vaccine is dried and tested on guinea-pigs.

Observation over five years of the frequency of cases among vaccinated and unvaccinated persons exposed to infection gave an average of 0.5% for the former, 12.3% for the latter. Vaccination was carried out in brucellosis areas on 200 000 persons, and among these the incidence of the disease was 3.3 times (in one instance 11.2 times) less than among the unvaccinated. Brucellosis even disappeared from some groups of workers exposed to infection when newly engaged staff were vaccinated on appointment. The vaccine is generally administered subcutaneously, but cutaneous administration seems to give just as good results. Revaccination is carried out a year afterwards to establish a solid immunity. To improve prophylactic methods still further, attempts are being made to find a method of cutaneous administration of general application, to perfect the process of lyophilization of the vaccine, and to isolate new strains of *Brucella* of higher immunogenicity.

[1] *Bull. Wld Hlth Org.*, 1961, 24 (In preparation)

Chemotherapy of malaria

The use of chemotherapy in malaria eradication programmes is no longer confined to those circumstances in which spraying with residual insecticides is either impracticable or relatively imperfect. Not only do antimalarial drugs play an essential part in the last phase of eradication when they are used, in conjunction with surveillance activities, for the diminution of the parasite reservoir and for quick action against imported infection, but it is now recognized that the time required to achieve complete interruption of transmission and elimination of the parasite reservoir may be considerably reduced by the judicious use of these drugs.

In areas where insecticides alone are fully effective in interrupting transmission, the use of drugs during the last year of the attack phase accelerates the success of the spraying campaign, and a single dose treatment is usually given to all suspected cases encountered during the surveillance activities introduced at that stage of the campaign. Chloroquine or amodiaquine are the drugs most often used, occasionally in association with pyrimethamine. The purpose of this treatment is not only to relieve clinical symptoms, but also to make the patient non-infective to mosquitos for a certain number of days.

Where, for various reasons, complete interruption of transmission by insecticides alone is difficult, mass administration of drugs may be required as a supplementary measure to residual spraying. It may take the form either of a single dose given to each member of the population at the time when house spraying is carried out, or of regular administration of drugs to the whole population, repeated at short intervals over a period.

After the successful completion of the attack phase the use of antimalarial drugs during the consolidation phase is of primary importance. During this phase " presumptive " (single dose) treatment of all suspected malaria cases and subsequent radical treatment of all confirmed cases to prevent relapses are the principal measures for eliminating residual infection and foci of transmission. The same applies to the maintenance phase, when drugs are also essential to prevent any new spread of disease from imported cases. The full treatment aiming at radical cure of all cases may encounter difficulties in many countries. While the radical cure of falciparum infections is relatively easy, the relapsing vivax and malariae infections require an additional treatment of 14 days with an 8-aminoquinoline (primaquine or quinocide) and some degree of medical supervision because of the potential toxicity of the drugs employed. So far only countries with well-developed rural health services have been able to carry out efficient radical treatment of most, or all, malaria cases. In certain areas which are difficult of access and where the population is widely scattered, the 14-day treatment with 8-aminoquinolines has been tentatively replaced by single doses of pyrimethamine given once monthly for 6 months or every 3 weeks during the transmission season. The value of this method has not been fully assessed.

Finally, there are circumstances which preclude the use of insecticides, as for example when the population is widely scattered in very large areas without communications. In these conditions chemotherapy may be the only method of attack and the most practicable way of administering it appears to be by adding antimalarials to the common household salt used by the population (Pinotti method). Chloroquine is now considered to be the most suitable drug for use in medicated salt. One of the main obstacles to the large-scale application of chloroquinized salt has been the difficulty of preparing a chloroquine salt mixture of adequate stability under conditions of high humidity in the tropics. There is now some evidence that a satisfactory solution to this problem may be found; this would make it possible to use medicated salt more efficiently and on a larger scale.

In general, it may be said that modern antimalarial drugs are adequate for suppression treatment and radical cure of malaria in individuals or small well-supervised groups. The exigencies of malaria eradication programmes, especially in developing countries, are such that the drugs available today often fall short of expectations, mainly because their adequate administration is difficult. All the present drugs have a relatively short " carry over " effect, and this is a serious drawback to the full use of antimalarials in many areas of the world. There is an urgent need for an antimalarial with a prolonged action on the pre-erythrocytic cycle of the development of the parasite in man, and for a long-acting schizonticide. These would facilitate administration, which could be no more than once every 3 or once every 6 months. New drugs are also required for the radical cure of relapsing vivax and malariae infections in order to shorten the time needed for the treatment. The best drug for this purpose would be an antimalarial with a full effect after a single dose or after a treatment not exceeding three days.

These problems were reviewed at a Technical Meeting on the Chemotherapy of Malaria convened by WHO, from 14 to 19 November 1960, in Geneva. The participants included research

workers in chemotherapy, malariologists, chemists, and industrial biologists.

Enteritis choleriformis in Indonesia

In 1905, vibrio strains were isolated from dead bodies of returned Mecca pilgrims at the quarantine camp of El Tor on the west coast of the Sinai Peninsula. Though these pilgrims had shown no signs of cholera, the vibrios were agglutinable with cholera-immune serum and in all other respects reacted in the same way as true cholera vibrios to the tests current at the time. However, it was discovered shortly afterwards that, unlike the true vibrio, they had haemolytic properties. There was subsequently much controversy about the relationship of these El Tor vibrios to the cholera vibrio, their pathogenic properties, and their presence and distribution in areas of endemic cholera.

In 1937-38, 1939-40 and 1944, a choleraic disease with a high fatality rate was observed in South Celebes. A study of 370 vibrio strains isolated from the patients permitted their identification as the El Tor type. Since then, as Pollitzer states,[1] " it would be unwise to deny the possibility that El-Tor-type vibrios can be responsible for occasional choleraic manifestations in man ". Further cases were reported in 1957 in the same area.

Two recent issues of the WHO *Weekly Epidemiological Record*[2] report new cases of enteritis choleriformis in Celebes. The first states that 60 deaths provisionally attributed to El-Tor-type paracholera occurred in the Gorontalo area of Sulawesi province (Celebes), Indonesia, in September 1960, and the second that 10 cases (8 of them fatal) were confirmed as positive for the El Tor vibrio. The Gorontalo area is situated in the north-eastern part of Celebes, whereas this type of infection had previously been reported mainly in the south of the island. The *Weekly Epidemiological Record* also mentions that 24 laboratory-confirmed cases with 13 deaths were reported in Makassar at the beginning of 1960, and 6 more cases between February and May 1960. A single fatal case was also reported in Djakarta in April 1960.

[1] Pollitzer, R. (1960) *Cholera* (*World Health Organization : Monograph Series*, No. 43), Geneva, p. 158

[2] *Wkly Epidem. Rec.*, 1960, 35, 446, 456

Risks involved in the laboratory diagnosis of tuberculosis

In the course of WHO/UNICEF tuberculosis surveys in a number of African territories, sputa were microscopically examined for the presence of acid-fast bacilli. Since adequate facilities were not available in these territories, specimens were sent to the WHO Tuberculosis Research Office in Prague for culturing and typing of mycobacteria. Considerable differences were noted between the results of the examinations before despatch and after arrival in Prague. A trial carried out to discover the reasons for this is described by L. Šula and co-workers in a recent number of the WHO Bulletin.[1]

Pure cultures of *Mycobacterium tuberculosis*, strain H37Rv, propagated in Dubos-Tween medium, centrifuged and resuspended in various dilutions of saline, were put in glass ampoules and plastic boxes. Some were kept at the Prague laboratory at 4°C, the others sent in insulated packing-cases to Entebbe, Uganda, where for 10 days they were submitted to changes of temperature and handling corresponding to what they would normally undergo during despatch to European laboratories. The temperature within the packing-cases was recorded automatically. It varied from 5°C to 11°C, and in one exceptional case went up to 25°C.

After being sent back to Prague, the specimens were cultured on various media and then compared with suspensions that had not undergone transport but had been kept at 4°C, and also with inoculations of fresh material made before the original despatch.

It was clearly shown that preservation adversely affects the viability of tubercle bacilli, but that transport is even more harmful and considerably lowers the cultivability of the bacilli. The same conclusion was drawn from a similar experiment with sputum specimens.

[1] Šula, L., Sundaresan, T. K. & Langerová, M. (1960) *Bull. Wld Hlth Org.*, 23, 635

The effects of storage and transport are not the only complicating factor in the laboratory diagnosis of tuberculosis. It has been observed for some time that there is a considerable variation between the proportion of positive cultures obtained at different laboratories from sputum specimens which were either positive or negative on microscopy. This was thought to be due to variations in the sensitivity of the culture media employed. To clarify the problem a comparative study was undertaken by the Prague Tuberculosis Research Institute, and the results are described by L. Šula and co-workers in the same number of the Bulletin.[2]

Various strains of tubercle bacilli were cultivated on the same medium—Löwenstein-Jensen (L-J)—prepared in different batches and at various stages in seven different laboratories, then inspissated in culture tubes or Petri dishes of different origins (Czechoslovak or Danish).

The results confirmed what had been suspected. The development of the same strain on L-J media prepared in different places was not identical. It even varied between two batches of media prepared in the same laboratory. The quality of the glassware appeared to have some influence on growth. Thus the L-J medium prepared at the Statens Seruminstitut, Copenhagen, and kept in Danish tubes proved to be the most sensitive. Next came the medium prepared in Prague, which was more sensitive in Danish than in Czechoslovak tubes. Growth was much more prolific in Petri dishes than in tubes. There was also less variation between Petri dishes of the same medium than between tubes of the same medium. This suggests that factors other than the nutrient value of the medium may affect its sensitivity.

It is therefore hardly possible to make valid comparisons between results obtained with cultures on L-J media, as long as each laboratory uses its own glassware and its own methods of preparation.

Water sanitation

An international refresher course on water sanitation was held by the WHO Regional Office for Europe, in co-operation with the Czechoslovak Government, in Prague from 17 October to 12 November 1960. It was attended by sanitary engineers and professional public health officials from Austria, Bulgaria, Czechoslovakia, France, Germany, Italy, Poland, Portugal, Spain, Switzerland, the USSR and Yugoslavia.

The course was intended to provide refresher training in all aspects of water sanitation, including the provision and purification of public supplies of potable water, and the prevention and control of pollution by domestic sewage and industrial wastes.

The first week of the course included field visits to research stations and sanitary installations in Bohemia and Moravia. During the remaining weeks, there were lectures, demonstrations, and laboratory work at the Institute of Hygiene, the Institute of Chemical Technology, and the research institutes of the Ministry of Agriculture, Water and Forests. The official language of the course was French, but through the courtesy of the Czechoslovak Government the lectures were simultaneously translated into Czech, German and Russian. Lectures were given by experts from Czechoslovakia, Switzerland, the United Kingdom, and WHO.

Expert Committee on Bilharziasis

The first report of the WHO Expert Committee on Bilharziasis [1] reviewed available knowledge of the geographical distribution and epidemiology of the disease, as well as survey methods. Subsequently WHO convened study groups on snail host identification and classification,[2] and on the ecology of the intermediate hosts,[3] as well as two African Conferences on Bilharziasis, one in 1956 [4] and one in 1960.[5] In connexion with the Organization's intensified programme of medical research, scientific groups on molluscicides, chemotherapy, and the assessment of the medical and public health importance of bilharziasis have been convened.

A WHO Expert Committee on Bilharziasis met in Geneva, from 26 September to 1 October 1960.

[2] Šula, L., Sundaresan, T. K. & Langerová, M. (1960) *Bull. Wld Hlth Org.*, 23, 653

[1] *Wld Hlth Org. techn. Rep. Ser.*, 1953, **65**
[2] *Wld Hlth Org. techn. Rep. Ser.*, 1954, **90**
[3] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **120**
[4] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **139**
[5] *Wld Hlth Org. techn. Rep. Ser.*, 1960, **204**

As it is commonly recognized that the elimination of the snail intermediate hosts is at present the most effective single method of controlling bilharziasis, and as new and improved molluscicides have been discovered in recent years, the Committee reviewed the role of molluscicides in bilharziasis control. Problems relating to the application of molluscicides under various ecological conditions were examined, and preliminary procedures recommended. Ways of obtaining the maximum results from molluscicides were also considered. The need for better compounds was discussed, and suggestions for their development put forward. Suggestions were also made on the development of new equipment for the application of chemicals.

An account of the Committee's work will be published in the Chronicle when its report appears.

Course on rural public health

The latest in a series of courses on rural public health, organized by the WHO Regional Office for Europe for doctors holding responsible positions in public health services, took place in the Soissons Public Health Centre, France, from 3 to 29 October 1960, under the joint auspices of the Regional Office and the National School of Public Health, Paris. This was the fourth French-language course in the series; the other three were held, also at the Soissons Centre, in 1955, 1956 and 1958. In addition, a similar course was held in English in the Uusimaa area of Finland in 1959.

The Soissons Public Health Centre is situated in a mainly rural district of the Aisne Department, about 60 miles north of Paris, and those attending the course were able to take part in field visits and demonstrations. The course opened with introductory lectures on public health work in France and the special characteristics of French rural areas. The following subjects were then studied: organization of medical care in rural areas, health statistics, antituberculosis work, maternal and child health, mental health, environmental sanitation, health education, geriatrics, anticancer work, rural occupational diseases, zoonoses, and the functions of the rural hospital. The work of international agencies in the field of rural health was also reviewed, with particular reference to the work of WHO.

The course was attended by 21 WHO or French Government fellows from countries in the African, Eastern Mediterranean and South-East Asia Regions.

Treatment of radiation injury

A Scientific Meeting on the Diagnosis and Treatment of Acute Radiation Injury was held in Geneva, from 17 to 21 October 1960, under the joint auspices of WHO and the International Atomic Energy Agency (IAEA). It was attended by 30 leading scientists from France, India, the Netherlands, Poland, the United Kingdom, the USA, the USSR, and Yugoslavia. The main topics discussed were: the acute radiation syndrome in man and its treatment; radiation given therapeutically and followed by tissue transplantation; and bone-marrow transplantation in man and animals.

While future radiation accidents may be of a different type from those experienced so far, the experts considered that certain features in the diagnosis and treatment of acute radiation injury will remain essentially unaltered. Clinical observation and acumen in both diagnosis and prognosis will continue to be important, particularly in view of the difficulties often met in assessing the radiation doses received. Important factors influencing the pathological processes following accidental irradiation are the parts of the body exposed, as well as the type of radiation and the rate at which it is delivered. Blood tests, in the opinion of the experts, are important in diagnosis, though there may be considerable variations among the persons involved, even in a single accident. It was agreed that a strict medical regimen should be adopted immediately, and that treatment should be undertaken according to the symptoms and signs as they arise.

Treatment by antibiotics and blood transfusion was discussed, as well as the possibility of "replacement therapy" whereby, for example, damaged bone marrow might be replaced.

The nurse and child care

A seminar on nursing education for child care was held in Vienna, from 14 to 23 November 1960, under the auspices of the WHO Regional Office for Europe and in collaboration with the

Government of Austria. It was the latest in a series of meetings started by the Regional Office in 1955 to study the functions of the nurse in general and specialized fields and her education in relation to modern concepts of nursing.

The meeting was organized in view of the great interest now shown in preparing the nurse for the care of the healthy as well as the sick child. In fact, increased knowledge of children's physical and emotional needs may make it necessary to redefine nursing responsibilities and techniques in the field of child care and to revise education programmes in this branch of nursing.

The seminar first discussed the influence of society and environment on the child and its parents, and then the evolution of the nursing care of children in Europe. New trends in the medical and psychological aspects of child care were reviewed, as well as the educational needs of the developing child in illness. The role of the children's nurse inside and outside the hospital and the selection and education of nurses for different types of child care were also examined.

The participants in the seminar included 38 nurses, paediatricians, child psychologists, psychiatrists, etc. selected by the Governments of Austria, Belgium, Bulgaria, Czechoslovakia, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland, Turkey, the United Kingdom, and Yugoslavia. In addition, the Regional Office invited some leading experts on paediatrics and paediatric nursing, education and child psychology to contribute their knowledge and experience to the work of the group.

Uses and abuses of X-ray examination

"The Committee felt strongly that chest X-ray examination by radiophotography or radiography is an extremely valuable tool in tuberculosis control and that the amount of radiation from properly constructed and properly operated machines used for such purposes is negligible compared with the benefits when chest X-ray examination is indicated. Nevertheless, the Committee advocated that every possible effort should be made to abolish all unnecessary radiation; it believed that fluoroscopy should not be used as a screening procedure, not only because of the greatly increased degree of radiation but also because it does not provide a permanent record for comparison with subsequent X-ray films. Whether or not tuberculin testing should precede X-ray examination of the chest in various population groups to reduce exposure to radiation would depend on local circumstances (i.e., the prevalence of tuberculous infection and disease) and therefore should be determined locally; but the Committee concurred with the general view that the examination of children in countries where the yield of cases is known to be low in this age-group should be confined to those first shown to have been naturally infected."

From the seventh report of the WHO Expert Committee on Tuberculosis (*Wld Hlth Org. techn. Rep. Ser.*, 1960, **195**)

Review of WHO Publications

LIVE POLIOVIRUS VACCINES

Live Poliovirus Vaccines. Papers Presented and Discussions Held at the Second International Conference on Live Poliovirus Vaccines (Pan American Sanitary Bureau, Regional Office for the Americas of the World Health Organization, Scientific Publication No. 50), Washington, D.C., 1960, 634 pages, illustrated. Price: $5.

Research on live poliovirus vaccines and experience of their use have developed so rapidly since the first international conference on this subject held in June 1959 that a second conference was held a year later to discuss and evaluate the most recent information. This took place in Washington, D.C., from 6 to 10 June 1960, under the auspices of the Pan American Health Organization and the World Health Organization, with the co-operation of the Sister Elizabeth Kenny Foundation, and was attended by experts from all over the world. The papers presented (with illustrations, tables and graphs), together with summaries and the subsequent discussions, have just been published in one volume.

These papers come under two general headings: safety, and efficacy. Under the first are grouped a number of studies on laboratory tests to assess the safety of the live vaccine: the multiplication of the vaccine virus in man, correlation between poliovirus markers and monkey neurovirulence, experimental studies on animals, viral agents in kidney-cell cultures of monkeys, etc. The safety of the vaccine in mass vaccination programmes is examined from various aspects: the spread of vaccine strains of poliovirus in the community, their capacity to cause infection, and results in the field.

The efficacy of the vaccine is reviewed on the basis of laboratory evidence on antibody response (taking into account the influence of age and the method of administration) and results in the field. There are new evaluations of the mass campaigns undertaken in various parts of the world—the Congo (Leopoldville), Costa Rica, Czechoslovakia, Finland, Nicaragua, Poland, the USA and the USSR. The volume concludes with a general summary of the work of the Conference, and an index.

MEDICAL SUPERVISION IN RADIATION WORK

Expert Committee on Radiation : Second Report (*World Health Organization Technical Report Series*, No. 196), Geneva, 1960, 31 pages. Price: 1/9, $0.30, or Sw. fr. 1.—.

A remarkable fact that is often not realized is that the effects of radiation have been studied in much greater detail than those of most other harmful physical or chemical agents to which workers are exposed. The knowledge obtained in this field over the years through contributions from radiobiology and radiation medicine has served as a basis for strikingly successful health protection programmes that have contributed substantially to the development of nuclear energy.

The physician is responsible for the medical side of the radiation health programme, including certain aspects of the selection of radiation workers, the regular evaluation of work assignments, and the diagnosis and treatment of radiation injury. In fulfilling these tasks he requires the co-operation of physicists and chemists expert in the measurement of radiation levels and analysis of radioactive materials, and of biologists familiar with the effects of radiation and the behaviour of radio elements in the body. All these tasks must be co-ordinated, and this can only be done through active and continuous team work.

The second report of the WHO Expert Com-

mittee on Radiation [1] examines exposure hazards in medical radiology, the medical application of radioisotopes, radiography and radioisotopes in industry, research uses of radiation and radioisotopes, and atomic energy activities, and then goes on to establish the aims of medical supervision in radiation work. These are: the protection of individual workers, the selection and assignment of personnel, medical care, and the maintenance of personal health.

To achieve these aims, the physician must take into account the data obtained from experimental studies and investigations of work environments, examine workers prior to and periodically during employment for any possible effects of radiation, and organize adequate services for the rapid treatment of lesions and diseases of occupational origin. If he is to fulfil his task satisfactorily, he must have special knowledge of radiation medicine—to the teaching of which WHO has devoted two technical reports.[2]

Among the factors to be taken into account in the selection of personnel for radiation work are age, sex, a history of hereditary defects, pre-existing disease, a previous radiation history, and certain special medical findings. The condition of the skin and blood receives particular mention. In examining the skin, special note should be taken of any signs of atrophy, multiple telangiectases, hyperkeratoses, brittleness and ridging of the nails, and chronic dermatoses. The blood should be carefully examined and attention paid to abnormal or excessive numbers of immature cells, instability of or wide fluctuations in the haematological elements on repeated examinations, and any apparent decrease in the number of, or the presence of abnormal characteristics in, the platelets. Laboratories should standardize their techniques and submit their results to critical analysis. Exclusion from radiation work should not be based on a single examination, since variations are often due to purely physiological fluctuations or to minor transitory causes.

The report also deals with the aims of subsequent medical examinations and the frequency with which these should be carried out. These periodic examinations should not only include routine procedures such as a clinical examination and clinical analysis of the urine and blood, but in certain cases also such special techniques as analysis of the excreta for radioactive substances. The report gives attention to the evaluation of the body-burden of radioactive elements, absorption and deposition of these elements being one of the greatest potential dangers to which some workers are exposed.

Details are given of the facilities that should be available for the examination and treatment of workers, including services for the decontamination of personnel who have suffered exposure to radioactive substances. The report does not describe in detail the care of persons seriously injured by radiation since this has been dealt with in other publications, but it gives some rules for first aid in cases of accident. Summarized, these rules call for: immediate removal of the patient from the radiation area; prompt expert assessment by a health physicist of the level of radiation exposure and of any contamination; closing off of the danger area and isolation of the patient, if contaminated, to prevent contamination of others; provisional determination of the type and degree of radiation exposure as a basis for treatment; cleaning of the patient to remove all readily removable radioactivity—this can be continued when the initial medical and surgical measures are applied; and bed for the patient until the diagnosis of actual or impending acute radiation syndrome has been confirmed or excluded. Routine blood counts should be taken, and all samples of the patient's blood, urine, faeces, vomitus and sputum, as well as his clothing, should be preserved for analysis. If exposure to more than 100 r is suspected, the patient should be transferred to hospital for observation and treatment as indicated.

[1] Members of the Committee: Dr M. N. Fateeva, USSR; Dr Asher J. Finkel, USA (Rapporteur); Dr B. Lindell, Sweden; Dr A. S. McLean, United Kingdom; Dr Carlo Polvani, Italy; Dr J. Reboul, France; Dr Ernest M. Renton, Canada; Dr James H. Sterner, USA (Chairman); Dr Katherine Williams, United Kingdom (Vice-Chairman). Representatives of United Nations agencies: Dr H. T. Daw, International Atomic Energy Agency; Dr R. Murray, International Labour Office; Mr E. Hellen, International Labour Office. Secretariat: Dr R. L. Dobson, WHO (Secretary); Dr H. Lisco, USA (Consultant); Dr P. Taillard, WHO; Dr B. M. Wheatley, European Organization for Nuclear Research (Consultant).

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1958, **154**, **155**